



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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<b>(21) International Application Number:</b> PCT/US00/08896 <b>(22) International Filing Date:</b> 3 April 2000 (03.04.00)  <b>(30) Priority Data:</b> <table border="0"> <tr> <td>09/285,479</td> <td>2 April 1999 (02.04.99)</td> <td>US</td> </tr> <tr> <td>09/466,396</td> <td>17 December 1999 (17.12.99)</td> <td>US</td> </tr> <tr> <td>09/476,496</td> <td>30 December 1999 (30.12.99)</td> <td>US</td> </tr> <tr> <td>09/480,884</td> <td>10 January 2000 (10.01.00)</td> <td>US</td> </tr> <tr> <td>09/510,376</td> <td>22 February 2000 (22.02.00)</td> <td>US</td> </tr> </table> <b>(71) Applicant (for all designated States except US):</b> CORIXA CORPORATION [US/US]; Suite 200, 1124 Columbia Street, Seattle, WA 98104 (US).  <b>(72) Inventors; and</b> <b>(75) Inventors/Applicants (for US only):</b> WANG, Tongtong [US/US]; 8049 NE 28th Street, Medina, WA 98039 (US). FAN, Liqun [CN/US]; 14116 SE 46th Street, Bellevue, WA 98006 (US).  <b>(74) Agents:</b> MAKI, David, J.; Seed Intellectual Property Law Group PLLC, Suite 6300, 701 Fifth Avenue, Seattle, WA 98104-7092 (US) et al.		09/285,479	2 April 1999 (02.04.99)	US	09/466,396	17 December 1999 (17.12.99)	US	09/476,496	30 December 1999 (30.12.99)	US	09/480,884	10 January 2000 (10.01.00)	US	09/510,376	22 February 2000 (22.02.00)	US	<b>(81) Designated States:</b> AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>Without international search report and to be republished upon receipt of that report.</i>
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<b>(54) Title:</b> COMPOUNDS AND METHODS FOR THERAPY AND DIAGNOSIS OF LUNG CANCER  <b>(57) Abstract</b> <p>Compounds and methods for the treatment and diagnosis of lung cancer are provided. The inventive compounds include polypeptides containing at least a portion of a lung tumor protein. Vaccines and pharmaceutical compositions for immunotherapy of lung cancer comprising such polypeptides, or DNA molecules encoding such polypeptides, are also provided, together with DNA molecules for preparing the inventive polypeptides.</p>																	

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## COMPOUNDS AND METHODS FOR THERAPY AND DIAGNOSIS OF LUNG CANCER

### TECHNICAL FIELD

5           The present invention relates generally to therapy and diagnosis of cancer, such as lung cancer. The invention is more specifically related to polypeptides comprising at least a portion of a lung tumor protein, and to polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides may be used in vaccines and pharmaceutical compositions for prevention and treatment of lung cancer, and for the  
10       diagnosis and monitoring of such cancers.

### BACKGROUND OF THE INVENTION

          Lung cancer is the primary cause of cancer death among both men and women in the U.S., with an estimated 172,000 new cases being reported in 1994. The five-year survival rate among all lung cancer patients, regardless of the stage of disease  
15       at diagnosis, is only 13%. This contrasts with a five-year survival rate of 46% among cases detected while the disease is still localized. However, only 16% of lung cancers are discovered before the disease has spread.

          Early detection is difficult since clinical symptoms are often not seen until the disease has reached an advanced stage. Currently, diagnosis is aided by the  
20       use of chest x-rays, analysis of the type of cells contained in sputum and fiberoptic examination of the bronchial passages. Treatment regimens are determined by the type and stage of the cancer, and include surgery, radiation therapy and/or chemotherapy. In spite of considerable research into therapies for the disease, lung cancer remains difficult to treat.

25           Accordingly, there remains a need in the art for improved vaccines, treatment methods and diagnostic techniques for lung cancer.

### SUMMARY OF THE INVENTION

          Briefly stated, the present invention provides compositions and methods for the diagnosis and therapy of cancer, such as lung cancer. In one aspect, the present

invention provides polypeptides comprising at least a portion of a lung tumor protein, or a variant thereof. Certain portions and other variants are immunogenic, such that the ability of the variant to react with antigen-specific antisera is not substantially diminished. Within certain embodiments, the polypeptide comprises a sequence that is encoded by a polynucleotide sequence selected from the group consisting of: (a) sequences recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253-337, 345, 347 and 349; (b) variants of a sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253-337, 345, 347 and 349; and (c) complements of a sequence of (a) or (b). In specific embodiments, the polypeptides of the present invention comprise at least a portion of a tumor protein that includes an amino acid sequence selected from the group consisting of sequences recited in any one of SEQ ID NO: 152, 155, 156, 165, 166, 169, 170, 172, 174, 176, 226-252, 338-344 and 346, and variants thereof.

The present invention further provides polynucleotides that encode a polypeptide as described above, or a portion thereof (such as a portion encoding at least 15 amino acid residues of a lung tumor protein), expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, vaccines for prophylactic or therapeutic use are provided. Such vaccines comprise a polypeptide or polynucleotide as described above and an immunostimulant.



The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a lung tumor protein; and (b) a physiologically acceptable carrier.

Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

Within related aspects, vaccines are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above, and (b) an immunostimulant.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

Within related aspects, pharmaceutical compositions comprising a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a physiologically acceptable carrier are provided.

Vaccines are further provided, within other aspects, that comprise a fusion protein, or a polynucleotide encoding a fusion protein, in combination with an immunostimulant.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as recited above.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a lung tumor protein, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated as described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a lung tumor protein, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Determined T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells determined from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of a lung tumor protein; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody. The cancer may be lung cancer.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the

sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a lung tumor protein; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a lung tumor protein; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

5

#### SEQUENCE IDENTIFIERS

- SEQ ID NO: 1 is the determined cDNA sequence for LST-S1-2  
SEQ ID NO: 2 is the determined cDNA sequence for LST-S1-28  
SEQ ID NO: 3 is the determined cDNA sequence for LST-S1-90  
10 SEQ ID NO: 4 is the determined cDNA sequence for LST-S1-144  
SEQ ID NO: 5 is the determined cDNA sequence for LST-S1-133  
SEQ ID NO: 6 is the determined cDNA sequence for LST-S1-169  
SEQ ID NO: 7 is the determined cDNA sequence for LST-S2-6  
SEQ ID NO: 8 is the determined cDNA sequence for LST-S2-11  
15 SEQ ID NO: 9 is the determined cDNA sequence for LST-S2-17  
SEQ ID NO: 10 is the determined cDNA sequence for LST-S2-25  
SEQ ID NO: 11 is the determined cDNA sequence for LST-S2-39  
SEQ ID NO: 12 is a first determined cDNA sequence for LST-S2-43  
SEQ ID NO: 13 is a second determined cDNA sequence for LST-S2-43  
20 SEQ ID NO: 14 is the determined cDNA sequence for LST-S2-65  
SEQ ID NO: 15 is the determined cDNA sequence for LST-S2-68  
SEQ ID NO: 16 is the determined cDNA sequence for LST-S2-72  
SEQ ID NO: 17 is the determined cDNA sequence for LST-S2-74  
SEQ ID NO: 18 is the determined cDNA sequence for LST-S2-103  
25 SEQ ID NO: 19 is the determined cDNA sequence for LST-S2-N1-1F  
SEQ ID NO: 20 is the determined cDNA sequence for LST-S2-N1-2A  
SEQ ID NO: 21 is the determined cDNA sequence for LST-S2-N1-4H  
SEQ ID NO: 22 is the determined cDNA sequence for LST-S2-N1-5A  
SEQ ID NO: 23 is the determined cDNA sequence for LST-S2-N1-6B  
30 SEQ ID NO: 24 is the determined cDNA sequence for LST-S2-N1-7B  
SEQ ID NO: 25 is the determined cDNA sequence for LST-S2-N1-7H

- SEQ ID NO: 26 is the determined cDNA sequence for LST-S2-N1-8A  
SEQ ID NO: 27 is the determined cDNA sequence for LST-S2-N1-8D  
SEQ ID NO: 28 is the determined cDNA sequence for LST-S2-N1-9A  
SEQ ID NO: 29 is the determined cDNA sequence for LST-S2-N1-9E  
5 SEQ ID NO: 30 is the determined cDNA sequence for LST-S2-N1-10A  
SEQ ID NO: 31 is the determined cDNA sequence for LST-S2-N1-10G  
SEQ ID NO: 32 is the determined cDNA sequence for LST-S2-N1-11A  
SEQ ID NO: 33 is the determined cDNA sequence for LST-S2-N1-12C  
SEQ ID NO: 34 is the determined cDNA sequence for LST-S2-N1-12E  
10 SEQ ID NO: 35 is the determined cDNA sequence for LST-S2-B1-3D  
SEQ ID NO: 36 is the determined cDNA sequence for LST-S2-B1-6C  
SEQ ID NO: 37 is the determined cDNA sequence for LST-S2-B1-5D  
SEQ ID NO: 38 is the determined cDNA sequence for LST-S2-B1-5F  
SEQ ID NO: 39 is the determined cDNA sequence for LST-S2-B1-6G  
15 SEQ ID NO: 40 is the determined cDNA sequence for LST-S2-B1-8A  
SEQ ID NO: 41 is the determined cDNA sequence for LST-S2-B1-8D  
SEQ ID NO: 42 is the determined cDNA sequence for LST-S2-B1-10A  
SEQ ID NO: 43 is the determined cDNA sequence for LST-S2-B1-9B  
SEQ ID NO: 44 is the determined cDNA sequence for LST-S2-B1-9F  
20 SEQ ID NO: 45 is the determined cDNA sequence for LST-S2-B1-12D  
SEQ ID NO: 46 is the determined cDNA sequence for LST-S2-I2-2B  
SEQ ID NO: 47 is the determined cDNA sequence for LST-S2-I2-5F  
SEQ ID NO: 48 is the determined cDNA sequence for LST-S2-I2-6B  
SEQ ID NO: 49 is the determined cDNA sequence for LST-S2-I2-7F  
25 SEQ ID NO: 50 is the determined cDNA sequence for LST-S2-I2-8G  
SEQ ID NO: 51 is the determined cDNA sequence for LST-S2-I2-9E  
SEQ ID NO: 52 is the determined cDNA sequence for LST-S2-I2-12B  
SEQ ID NO: 53 is the determined cDNA sequence for LST-S2-H2-2C  
SEQ ID NO: 54 is the determined cDNA sequence for LST-S2-H2-1G  
30 SEQ ID NO: 55 is the determined cDNA sequence for LST-S2-H2-4G  
SEQ ID NO: 56 is the determined cDNA sequence for LST-S2-H2-3H

- SEQ ID NO: 57 is the determined cDNA sequence for LST-S2-H2-5G  
SEQ ID NO: 58 is the determined cDNA sequence for LST-S2-H2-9B  
SEQ ID NO: 59 is the determined cDNA sequence for LST-S2-H2-10H  
SEQ ID NO: 60 is the determined cDNA sequence for LST-S2-H2-12D  
5 SEQ ID NO: 61 is the determined cDNA sequence for LST-S3-2  
SEQ ID NO: 62 is the determined cDNA sequence for LST-S3-4  
SEQ ID NO: 63 is the determined cDNA sequence for LST-S3-7  
SEQ ID NO: 64 is the determined cDNA sequence for LST-S3-8  
SEQ ID NO: 65 is the determined cDNA sequence for LST-S3-12  
10 SEQ ID NO: 66 is the determined cDNA sequence for LST-S3-13  
SEQ ID NO: 67 is the determined cDNA sequence for LST-S3-14  
SEQ ID NO: 68 is the determined cDNA sequence for LST-S3-16  
SEQ ID NO: 69 is the determined cDNA sequence for LST-S3-21  
SEQ ID NO: 70 is the determined cDNA sequence for LST-S3-22  
15 SEQ ID NO: 71 is the determined cDNA sequence for LST-S1-7  
SEQ ID NO: 72 is the determined cDNA sequence for LST-S1-A-1E  
SEQ ID NO: 73 is the determined cDNA sequence for LST-S1-A-1G  
SEQ ID NO: 74 is the determined cDNA sequence for LST-S1-A-3E  
SEQ ID NO: 75 is the determined cDNA sequence for LST-S1-A-4E  
20 SEQ ID NO: 76 is the determined cDNA sequence for LST-S1-A-6D  
SEQ ID NO: 77 is the determined cDNA sequence for LST-S1-A-8D  
SEQ ID NO: 78 is the determined cDNA sequence for LST-S1-A-10A  
SEQ ID NO: 79 is the determined cDNA sequence for LST-S1-A-10C  
SEQ ID NO: 80 is the determined cDNA sequence for LST-S1-A-9D  
25 SEQ ID NO: 81 is the determined cDNA sequence for LST-S1-A-10D  
SEQ ID NO: 82 is the determined cDNA sequence for LST-S1-A-9H  
SEQ ID NO: 83 is the determined cDNA sequence for LST-S1-A-11D  
SEQ ID NO: 84 is the determined cDNA sequence for LST-S1-A-12D  
SEQ ID NO: 85 is the determined cDNA sequence for LST-S1-A-11E  
30 SEQ ID NO: 86 is the determined cDNA sequence for LST-S1-A-12E  
SEQ ID NO: 87 is the determined cDNA sequence for L513S (T3).

SEQ ID NO: 88 is the determined cDNA sequence for L513S contig 1.

SEQ ID NO: 89 is a first determined cDNA sequence for L514S.

SEQ ID NO: 90 is a second determined cDNA sequence for L514S.

SEQ ID NO: 91 is a first determined cDNA sequence for L516S.

5 SEQ ID NO: 92 is a second determined cDNA sequence for L516S.

SEQ ID NO: 93 is the determined cDNA sequence for L517S.

SEQ ID NO: 94 is the extended cDNA sequence for LST-S1-169 (also known as L519S).

SEQ ID NO: 95 is a first determined cDNA sequence for L520S.

10 SEQ ID NO: 96 is a second determined cDNA sequence for L520S.

SEQ ID NO: 97 is a first determined cDNA sequence for L521S.

SEQ ID NO: 98 is a second determined cDNA sequence for L521S.

SEQ ID NO: 99 is the determined cDNA sequence for L522S.

SEQ ID NO: 100 is the determined cDNA sequence for L523S.

15 SEQ ID NO: 101 is the determined cDNA sequence for L524S.

SEQ ID NO: 102 is the determined cDNA sequence for L525S.

SEQ ID NO: 103 is the determined cDNA sequence for L526S.

SEQ ID NO: 104 is the determined cDNA sequence for L527S.

SEQ ID NO: 105 is the determined cDNA sequence for L528S.

20 SEQ ID NO: 106 is the determined cDNA sequence for L529S.

SEQ ID NO: 107 is a first determined cDNA sequence for L530S.

SEQ ID NO: 108 is a second determined cDNA sequence for L530S.

SEQ ID NO: 109 is the determined full-length cDNA sequence for L531S short form

SEQ ID NO: 110 is the predicted amino acid sequence encoded by SEQ ID NO: 109.

25 SEQ ID NO: 111 is the determined full-length cDNA sequence for L531S long form

SEQ ID NO: 112 is the predicted amino acid sequence encoded by SEQ ID NO: 111.

SEQ ID NO: 113 is the determined full-length cDNA sequence for L520S.

SEQ ID NO: 114 is the predicted amino acid sequence encoded by SEQ ID NO: 113.

SEQ ID NO: 115 is the determined cDNA sequence for contig 1.

30 SEQ ID NO: 116 is the determined cDNA sequence for contig 3.

SEQ ID NO: 117 is the determined cDNA sequence for contig 4.

- SEQ ID NO: 118 is the determined cDNA sequence for contig 5.
- SEQ ID NO: 119 is the determined cDNA sequence for contig 7.
- SEQ ID NO: 120 is the determined cDNA sequence for contig 8.
- SEQ ID NO: 121 is the determined cDNA sequence for contig 9.
- 5 SEQ ID NO: 122 is the determined cDNA sequence for contig 10.
- SEQ ID NO: 123 is the determined cDNA sequence for contig 12.
- SEQ ID NO: 124 is the determined cDNA sequence for contig 11.
- SEQ ID NO: 125 is the determined cDNA sequence for contig 13.
- SEQ ID NO: 126 is the determined cDNA sequence for contig 15.
- 10 SEQ ID NO: 127 is the determined cDNA sequence for contig 16.
- SEQ ID NO: 128 is the determined cDNA sequence for contig 17.
- SEQ ID NO: 129 is the determined cDNA sequence for contig 19.
- SEQ ID NO: 130 is the determined cDNA sequence for contig 20.
- SEQ ID NO: 131 is the determined cDNA sequence for contig 22.
- 15 SEQ ID NO: 132 is the determined cDNA sequence for contig 24.
- SEQ ID NO: 133 is the determined cDNA sequence for contig 29.
- SEQ ID NO: 134 is the determined cDNA sequence for contig 31.
- SEQ ID NO: 135 is the determined cDNA sequence for contig 33.
- SEQ ID NO: 136 is the determined cDNA sequence for contig 38.
- 20 SEQ ID NO: 137 is the determined cDNA sequence for contig 39.
- SEQ ID NO: 138 is the determined cDNA sequence for contig 41.
- SEQ ID NO: 139 is the determined cDNA sequence for contig 43.
- SEQ ID NO: 140 is the determined cDNA sequence for contig 44.
- SEQ ID NO: 141 is the determined cDNA sequence for contig 45.
- 25 SEQ ID NO: 142 is the determined cDNA sequence for contig 47.
- SEQ ID NO: 143 is the determined cDNA sequence for contig 48.
- SEQ ID NO: 144 is the determined cDNA sequence for contig 49.
- SEQ ID NO: 145 is the determined cDNA sequence for contig 50.
- SEQ ID NO: 146 is the determined cDNA sequence for contig 53.
- 30 SEQ ID NO: 147 is the determined cDNA sequence for contig 54.
- SEQ ID NO: 148 is the determined cDNA sequence for contig 56.



- SEQ ID NO: 149 is the determined cDNA sequence for contig 57.
- SEQ ID NO: 150 is the determined cDNA sequence for contig 58.
- SEQ ID NO: 151 is the full-length cDNA sequence for L530S.
- SEQ ID NO: 152 is the amino acid sequence encoded by SEQ ID NO: 151
- 5 SEQ ID NO: 153 is the full-length cDNA sequence of a first variant of L514S
- SEQ ID NO: 154 is the full-length cDNA sequence of a second variant of L514S
- SEQ ID NO: 155 is the amino acid sequence encoded by SEQ ID NO: 153.
- SEQ ID NO: 156 is the amino acid sequence encoded by SEQ ID NO: 154.
- SEQ ID NO: 157 is the determined cDNA sequence for contig 59.
- 10 SEQ ID NO: 158 is the full-length cDNA sequence for L763P (also referred to as contig 22).
- SEQ ID NO: 159 is the amino acid sequence encoded by SEQ ID NO: 158.
- SEQ ID NO: 160 is the full-length cDNA sequence for L762P (also referred to as contig 17).
- 15 SEQ ID NO: 161 is the amino acid sequence encoded by SEQ ID NO: 160.
- SEQ ID NO: 162 is the determined cDNA sequence for L515S.
- SEQ ID NO: 163 is the full-length cDNA sequence of a first variant of L524S.
- SEQ ID NO: 164 is the full-length cDNA sequence of a second variant of L524S.
- SEQ ID NO: 165 is the amino acid sequence encoded by SEQ ID NO: 163.
- 20 SEQ ID NO: 166 is the amino acid sequence encoded by SEQ ID NO: 164.
- SEQ ID NO: 167 is the full-length cDNA sequence of a first variant of L762P.
- SEQ ID NO: 168 is the full-length cDNA sequence of a second variant of L762P.
- SEQ ID NO: 169 is the amino acid sequence encoded by SEQ ID NO: 167.
- SEQ ID NO: 170 is the amino acid sequence encoded by SEQ ID NO: 168.
- 25 SEQ ID NO: 171 is the full-length cDNA sequence for L773P (also referred to as contig 56).
- SEQ ID NO: 172 is the amino acid sequence encoded by SEQ ID NO: 171.
- SEQ ID NO: 173 is an extended cDNA sequence for L519S.
- SEQ ID NO: 174 is the predicted amino acid sequence encoded by SEQ ID NO: 174.
- 30 SEQ ID NO: 175 is the full-length cDNA sequence for L523S.
- SEQ ID NO: 176 is the predicted amino acid sequence encoded by SEQ ID NO: 175.

- SEQ ID NO: 177 is the determined cDNA sequence for LST-sub5-7A.  
SEQ ID NO: 178 is the determined cDNA sequence for LST-sub5-8G.  
SEQ ID NO: 179 is the determined cDNA sequence for LST-sub5-8H.  
SEQ ID NO: 180 is the determined cDNA sequence for LST-sub5-10B.  
5 SEQ ID NO: 181 is the determined cDNA sequence for LST-sub5-10H.  
SEQ ID NO: 182 is the determined cDNA sequence for LST-sub5-12B.  
SEQ ID NO: 183 is the determined cDNA sequence for LST-sub5-11C.  
SEQ ID NO: 184 is the determined cDNA sequence for LST-sub6-1c.  
SEQ ID NO: 185 is the determined cDNA sequence for LST-sub6-2f.  
10 SEQ ID NO: 186 is the determined cDNA sequence for LST-sub6-2G.  
SEQ ID NO: 187 is the determined cDNA sequence for LST-sub6-4d.  
SEQ ID NO: 188 is the determined cDNA sequence for LST-sub6-4e.  
SEQ ID NO: 189 is the determined cDNA sequence for LST-sub6-4f.  
SEQ ID NO: 190 is the determined cDNA sequence for LST-sub6-3h.  
15 SEQ ID NO: 191 is the determined cDNA sequence for LST-sub6-5d.  
SEQ ID NO: 192 is the determined cDNA sequence for LST-sub6-5h.  
SEQ ID NO: 193 is the determined cDNA sequence for LST-sub6-6h.  
SEQ ID NO: 194 is the determined cDNA sequence for LST-sub6-7a.  
SEQ ID NO: 195 is the determined cDNA sequence for LST-sub6-8a.  
20 SEQ ID NO: 196 is the determined cDNA sequence for LST-sub6-7d.  
SEQ ID NO: 197 is the determined cDNA sequence for LST-sub6-7e.  
SEQ ID NO: 198 is the determined cDNA sequence for LST-sub6-8e.  
SEQ ID NO: 199 is the determined cDNA sequence for LST-sub6-7g.  
SEQ ID NO: 200 is the determined cDNA sequence for LST-sub6-9f.  
25 SEQ ID NO: 201 is the determined cDNA sequence for LST-sub6-9h.  
SEQ ID NO: 202 is the determined cDNA sequence for LST-sub6-11b.  
SEQ ID NO: 203 is the determined cDNA sequence for LST-sub6-11c.  
SEQ ID NO: 204 is the determined cDNA sequence for LST-sub6-12c.  
SEQ ID NO: 205 is the determined cDNA sequence for LST-sub6-12e.  
30 SEQ ID NO: 206 is the determined cDNA sequence for LST-sub6-12f.  
SEQ ID NO: 207 is the determined cDNA sequence for LST-sub6-11g.

- SEQ ID NO: 208 is the determined cDNA sequence for LST-sub6-12g.  
SEQ ID NO: 209 is the determined cDNA sequence for LST-sub6-12h.  
SEQ ID NO: 210 is the determined cDNA sequence for LST-sub6-II-1a.  
SEQ ID NO: 211 is the determined cDNA sequence for LST-sub6-II-2b.  
5 SEQ ID NO: 212 is the determined cDNA sequence for LST-sub6-II-2g.  
SEQ ID NO: 213 is the determined cDNA sequence for LST-sub6-II-1h.  
SEQ ID NO: 214 is the determined cDNA sequence for LST-sub6-II-4a.  
SEQ ID NO: 215 is the determined cDNA sequence for LST-sub6-II-4b.  
SEQ ID NO: 216 is the determined cDNA sequence for LST-sub6-II-3e.  
10 SEQ ID NO: 217 is the determined cDNA sequence for LST-sub6-II-4f.  
SEQ ID NO: 218 is the determined cDNA sequence for LST-sub6-II-4g.  
SEQ ID NO: 219 is the determined cDNA sequence for LST-sub6-II-4h.  
SEQ ID NO: 220 is the determined cDNA sequence for LST-sub6-II-5c.  
SEQ ID NO: 221 is the determined cDNA sequence for LST-sub6-II-5e.  
15 SEQ ID NO: 222 is the determined cDNA sequence for LST-sub6-II-6f.  
SEQ ID NO: 223 is the determined cDNA sequence for LST-sub6-II-5g.  
SEQ ID NO: 224 is the determined cDNA sequence for LST-sub6-II-6g.  
SEQ ID NO: 225 is the amino acid sequence for L528S.  
SEQ ID NO: 226-251 are synthetic peptides derived from L762P.  
20 SEQ ID NO: 252 is the expressed amino acid sequence of L514S.  
SEQ ID NO: 253 is the DNA sequence corresponding to SEQ ID NO: 252.  
SEQ ID NO: 254 is the DNA sequence of a L762P expression construct.  
SEQ ID NO: 255 is the determined cDNA sequence for clone 23785.  
SEQ ID NO: 256 is the determined cDNA sequence for clone 23786.  
25 SEQ ID NO: 257 is the determined cDNA sequence for clone 23788.  
SEQ ID NO: 258 is the determined cDNA sequence for clone 23790.  
SEQ ID NO: 259 is the determined cDNA sequence for clone 23793.  
SEQ ID NO: 260 is the determined cDNA sequence for clone 23794.  
SEQ ID NO: 261 is the determined cDNA sequence for clone 23795.  
30 SEQ ID NO: 262 is the determined cDNA sequence for clone 23796.  
SEQ ID NO: 263 is the determined cDNA sequence for clone 23797.

- SEQ ID NO: 264 is the determined cDNA sequence for clone 23798.  
SEQ ID NO: 265 is the determined cDNA sequence for clone 23799.  
SEQ ID NO: 266 is the determined cDNA sequence for clone 23800.  
SEQ ID NO: 267 is the determined cDNA sequence for clone 23802.  
5 SEQ ID NO: 268 is the determined cDNA sequence for clone 23803.  
SEQ ID NO: 269 is the determined cDNA sequence for clone 23804.  
SEQ ID NO: 270 is the determined cDNA sequence for clone 23805.  
SEQ ID NO: 271 is the determined cDNA sequence for clone 23806.  
SEQ ID NO: 272 is the determined cDNA sequence for clone 23807.  
10 SEQ ID NO: 273 is the determined cDNA sequence for clone 23808.  
SEQ ID NO: 274 is the determined cDNA sequence for clone 23809.  
SEQ ID NO: 275 is the determined cDNA sequence for clone 23810.  
SEQ ID NO: 276 is the determined cDNA sequence for clone 23811.  
SEQ ID NO: 277 is the determined cDNA sequence for clone 23812.  
15 SEQ ID NO: 278 is the determined cDNA sequence for clone 23813.  
SEQ ID NO: 279 is the determined cDNA sequence for clone 23815.  
SEQ ID NO: 280 is the determined cDNA sequence for clone 25298.  
SEQ ID NO: 281 is the determined cDNA sequence for clone 25299.  
SEQ ID NO: 282 is the determined cDNA sequence for clone 25300.  
20 SEQ ID NO: 283 is the determined cDNA sequence for clone 25301  
SEQ ID NO: 284 is the determined cDNA sequence for clone 25304  
SEQ ID NO: 285 is the determined cDNA sequence for clone 25309.  
SEQ ID NO: 286 is the determined cDNA sequence for clone 25312.  
SEQ ID NO: 287 is the determined cDNA sequence for clone 25317.  
25 SEQ ID NO: 288 is the determined cDNA sequence for clone 25321.  
SEQ ID NO: 289 is the determined cDNA sequence for clone 25323.  
SEQ ID NO: 290 is the determined cDNA sequence for clone 25327.  
SEQ ID NO: 291 is the determined cDNA sequence for clone 25328.  
SEQ ID NO: 292 is the determined cDNA sequence for clone 25332.  
30 SEQ ID NO: 293 is the determined cDNA sequence for clone 25333.  
SEQ ID NO: 294 is the determined cDNA sequence for clone 25336.

- SEQ ID NO: 295 is the determined cDNA sequence for clone 25340.  
SEQ ID NO: 296 is the determined cDNA sequence for clone 25342.  
SEQ ID NO: 297 is the determined cDNA sequence for clone 25356.  
SEQ ID NO: 298 is the determined cDNA sequence for clone 25357.  
5 SEQ ID NO: 299 is the determined cDNA sequence for clone 25361.  
SEQ ID NO: 300 is the determined cDNA sequence for clone 25363.  
SEQ ID NO: 301 is the determined cDNA sequence for clone 25397.  
SEQ ID NO: 302 is the determined cDNA sequence for clone 25402.  
SEQ ID NO: 303 is the determined cDNA sequence for clone 25403.  
10 SEQ ID NO: 304 is the determined cDNA sequence for clone 25405.  
SEQ ID NO: 305 is the determined cDNA sequence for clone 25407.  
SEQ ID NO: 306 is the determined cDNA sequence for clone 25409.  
SEQ ID NO: 307 is the determined cDNA sequence for clone 25396.  
SEQ ID NO: 308 is the determined cDNA sequence for clone 25414.  
15 SEQ ID NO: 309 is the determined cDNA sequence for clone 25410.  
SEQ ID NO: 310 is the determined cDNA sequence for clone 25406.  
SEQ ID NO: 311 is the determined cDNA sequence for clone 25306.  
SEQ ID NO: 312 is the determined cDNA sequence for clone 25362.  
SEQ ID NO: 313 is the determined cDNA sequence for clone 25360.  
20 SEQ ID NO: 314 is the determined cDNA sequence for clone 25398.  
SEQ ID NO: 315 is the determined cDNA sequence for clone 25355.  
SEQ ID NO: 316 is the determined cDNA sequence for clone 25351.  
SEQ ID NO: 317 is the determined cDNA sequence for clone 25331.  
SEQ ID NO: 318 is the determined cDNA sequence for clone 25338.  
25 SEQ ID NO: 319 is the determined cDNA sequence for clone 25335.  
SEQ ID NO: 320 is the determined cDNA sequence for clone 25329.  
SEQ ID NO: 321 is the determined cDNA sequence for clone 25324.  
SEQ ID NO: 322 is the determined cDNA sequence for clone 25322.  
SEQ ID NO: 323 is the determined cDNA sequence for clone 25319.  
30 SEQ ID NO: 324 is the determined cDNA sequence for clone 25316.  
SEQ ID NO: 325 is the determined cDNA sequence for clone 25311.

- SEQ ID NO: 326 is the determined cDNA sequence for clone 25310.  
SEQ ID NO: 327 is the determined cDNA sequence for clone 25302.  
SEQ ID NO: 328 is the determined cDNA sequence for clone 25315.  
SEQ ID NO: 329 is the determined cDNA sequence for clone 25308.  
5 SEQ ID NO: 330 is the determined cDNA sequence for clone 25303.  
SEQ ID NO: 331-337 are the cDNA sequences of isoforms of the p53 tumor suppressor homologue, p63 (also referred to as L530S).  
SEQ ID NO: 338-344 are the amino acid sequences encoded by SEQ ID NO: 331-337, respectively.  
10 SEQ ID NO: 345 is a second cDNA sequence for the antigen L763P.  
SEQ ID NO: 346 is the amino acid sequence encoded by the sequence of SEQ ID NO: 345.  
SEQ ID NO: 347 is a determined full-length cDNA sequence for L523S.  
SEQ ID NO: 348 is the predicted amino acid sequence encoded by SEQ ID NO: 347.  
15 SEQ ID NO: 349 is the cDNA sequence encoding the N-terminal portion of L773P.  
SEQ ID NO: 350 is the amino acid sequence of the N-terminal portion of L773P.

#### DETAILED DESCRIPTION OF THE INVENTION

- As noted above, the present invention is generally directed to  
20 compositions and methods for the therapy and diagnosis of cancer, such as lung cancer.  
The compositions described herein may include lung tumor polypeptides, polynucleotides encoding such polypeptides, binding agents such as antibodies, antigen presenting cells (APCs) and/or immune system cells (*e.g.*, T cells). Polypeptides of the present invention generally comprise at least a portion (such as an immunogenic  
25 portion) of a lung tumor protein or a variant thereof. A "lung tumor protein" is a protein that is expressed in lung tumor cells at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in a normal tissue, as determined using a representative assay provided herein. Certain lung tumor proteins are tumor proteins that react detectably (within an immunoassay, such as an ELISA or Western  
30 blot) with antisera of a patient afflicted with lung cancer. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of

such a polypeptide, or that is complementary to such a sequence. Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to a polypeptide as described above. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B-cells that express a polypeptide as described above. T cells that may be employed within such compositions are generally T cells that are specific for a polypeptide as described above.

The present invention is based on the discovery human lung tumor proteins. Sequences of polynucleotides encoding specific tumor proteins are provided in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349.

#### LUNG TUMOR PROTEIN POLYNUCLEOTIDES

Any polynucleotide that encodes a lung tumor protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides and more preferably at least 45 consecutive nucleotides, that encode a portion of a lung tumor protein. More preferably, a polynucleotide encodes an immunogenic portion of a lung tumor protein. Polynucleotides complementary to any such sequences are also encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a lung tumor protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the immunogenicity of the

encoded polypeptide is not diminished, relative to a native tumor protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native lung tumor protein or a portion thereof. The term “variants” also encompasses homologous genes of xenogenic origin.

Two polynucleotide or polypeptide sequences are said to be “identical” if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A “comparison window” as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) *Atlas of Protein Sequence and Structure*, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad., Sci. USA* 80:726-730.

Preferably, the “percentage of sequence identity” is determined by comparing two optimally aligned sequences over a window of comparison of at least 20



positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (i.e. gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (i.e. the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are capable of hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native lung tumor protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that

is at least two fold greater in a lung tumor than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and  
5 Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Alternatively, polypeptides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as lung tumor cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

10 An amplified portion may be used to isolate a full length gene from a suitable library (e.g., a lung tumor cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be  
15 preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (e.g., by nick-translation or end-labeling with  $^{32}\text{P}$ ) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured  
20 bacterial colonies (or lawns containing phage plaques) with the labeled probe (see Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using  
25 a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into a single contiguous sequence. A full length cDNA molecule can be  
30 generated by ligating suitable fragments, using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

One such amplification technique is inverse PCR (*see* Triglia et al., *Nucl. Acids Res.* 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic.* 1:111-19, 1991) and walking PCR (Parker et al., *Nucl. Acids Res.* 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (*e.g.*, NCBI BLAST searches), and such ESTs

may be used to generate a contiguous full length sequence. Full length DNA sequences may also be obtained by analysis of genomic fragments.

Certain nucleic acid sequences of cDNA molecules encoding portions of lung tumor proteins are provided in SEQ ID NO: 1-109, 111, 113, 115-151, 153,  
5 154,157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349.

Polynucleotide variants may generally be prepared by any method known in the art, including chemical synthesis by, for example, solid phase phosphoramidite chemical synthesis. Modifications in a polynucleotide sequence may  
10 also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (*see* Adelman et al., *DNA* 2:183, 1983). Alternatively, RNA molecules may be generated by *in vitro* or *in vivo* transcription of DNA sequences encoding a lung tumor protein, or portion thereof, provided that the DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as  
15 T7 or SP6). Certain portions may be used to prepare an encoded polypeptide, as described herein. In addition, or alternatively, a portion may be administered to a patient such that the encoded polypeptide is generated *in vivo* (*e.g.*, by transfecting antigen-presenting cells, such as dendritic cells, with a cDNA construct encoding a lung tumor polypeptide, and administering the transfected cells to the patient).

20 A portion of a sequence complementary to a coding sequence (*i.e.*, an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs that can be transcribed into antisense RNA may also be introduced into cells of tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of a tumor  
25 protein. Antisense technology can be used to control gene expression through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors or regulatory molecules (*see* Gee et al., *In* Huber and Carr, *Molecular and Immunologic Approaches*, Futura Publishing Co. (Mt. Kisco, NY; 1994)). Alternatively, an antisense molecule may be designed to  
30 hybridize with a control region of a gene (*e.g.*, promoter, enhancer or transcription

initiation site), and block transcription of the gene; or to block translation by inhibiting binding of a transcript to ribosomes.

A portion of a coding sequence, or of a complementary sequence, may also be designed as a probe or primer to detect gene expression. Probes may be labeled  
5 with a variety of reporter groups, such as radionuclides and enzymes, and are preferably at least 10 nucleotides in length, more preferably at least 20 nucleotides in length and still more preferably at least 30 nucleotides in length. Primers, as noted above, are preferably 22-30 nucleotides in length.

Any polynucleotide may be further modified to increase stability *in vivo*.  
10 Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl- methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

15 Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques. For example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include expression vectors, replication vectors, probe generation  
20 vectors and sequencing vectors. In general, a vector will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

Within certain embodiments, polynucleotides may be formulated so as to  
25 permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not  
30 limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (e.g., avian pox virus). ). The polynucleotides may also be administered as naked

plasmid vectors. Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary skill in the art.

Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle *in vitro* and *in vivo* is a liposome (*i.e.*, an artificial membrane vesicle). The preparation and use of such systems is well known in the art.

#### 15 LUNG TUMOR POLYPEPTIDES

Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of a lung tumor protein or a variant thereof, as described herein. As noted above, a "lung tumor protein" is a protein that is expressed by lung tumor cells. Proteins that are lung tumor proteins also react detectably within an immunoassay (such as an ELISA) with antisera from a patient with lung cancer. Polypeptides as described herein may be of any length. Additional sequences derived from the native protein and/or heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

An "immunogenic portion," as used herein is a portion of a protein that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of a lung tumor protein or a variant thereof. Certain preferred immunogenic portions include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other preferred immunogenic portions may

contain a small N- and/or C-terminal deletion (e.g., 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-  
5 247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (i.e., they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins).  
10 Such antisera and antibodies may be prepared as described herein, and using well known techniques. An immunogenic portion of a native lung tumor protein is a portion that reacts with such antisera and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (e.g., in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is  
15 similar to or greater than the reactivity of the full length polypeptide. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the  
20 sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, <sup>125</sup>I-labeled Protein A.

As noted above, a composition may comprise a variant of a native lung tumor protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native lung tumor protein in one or more substitutions, deletions, additions  
25 and/or insertions, such that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with antigen-specific antisera may be enhanced or unchanged, relative to the native protein, or may be diminished by less than 50%, and preferably less than 20%, relative to the native protein. Such variants may generally be identified by modifying one of the above  
30 polypeptide sequences and evaluating the reactivity of the modified polypeptide with antigen-specific antibodies or antisera as described herein. Preferred variants include

those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein.

5 Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described above) to the identified polypeptides.

Preferably, a variant contains conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydropathic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydropathic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the



polypeptide (*e.g.*, poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

Polypeptides may be prepared using any of a variety of well known techniques. Recombinant polypeptides encoded by DNA sequences as described above may be readily prepared from the DNA sequences using any of a variety of expression  
5 vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast, higher eukaryotic and plant cells. Preferably, the host  
10 cells employed are *E. coli*, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or  
15 more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide.

Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example,  
20 such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems  
25 Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

Within certain specific embodiments, a polypeptide may be a fusion protein that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known  
30 tumor protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans,

or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be  
5 targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a recombinant protein, allowing the production of increased levels, relative to a non-fused  
10 protein, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase.  
15 This permits translation into a single fusion protein that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is  
20 incorporated into the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with  
25 the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S.  
30 Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second

polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (*see, for example, Stoute et al. New Engl. J. Med., 336:86-91, 1997*).

Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium *Haemophilus influenza B* (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (*e.g.*, the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as amidase LYTA (encoded by the *LytA* gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible

for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (*see* 5 *Biotechnology* 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

In general, polypeptides (including fusion proteins) and polynucleotides 10 as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is 15 considered to be isolated if, for example, it is cloned into a vector that is not a part of the natural environment.

#### BINDING AGENTS

The present invention further provides agents, such as antibodies and 20 antigen-binding fragments thereof, that specifically bind to a lung tumor protein. As used herein, an antibody, or antigen-binding fragment thereof, is said to "specifically bind" to a lung tumor protein if it reacts at a detectable level (within, for example, an ELISA) with a lung tumor protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association 25 between two separate molecules such that a complex is formed. The ability to bind may be evaluated by, for example, determining a binding constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding 30 constant for complex formation exceeds about  $10^3$  L/mol. The binding constant may be determined using methods well known in the art.

Binding agents may be further capable of differentiating between patients with and without a cancer, such as lung cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a lung tumor protein will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (*e.g.*, blood, sera, sputum urine and/or tumor biopsies ) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the disease should be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. *See, e.g.*, Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (*e.g.*, mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically.

Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest  
5 may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (*i.e.*, reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as  
10 described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid  
15 cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

20 Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by  
25 conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

Within certain embodiments, the use of antigen-binding fragments of antibodies may be preferred. Such fragments include Fab fragments, which may be  
30 prepared using standard techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane,

*Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or  
5 more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include  $^{90}\text{Y}$ ,  $^{123}\text{I}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{211}\text{At}$ , and  $^{212}\text{Bi}$ . Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diphtheria  
10 toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, *Shigella* toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a  
15 substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an  
20 antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents,  
25 which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups,  
30 sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (*e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (*e.g.*, U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (*e.g.*, U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.



A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

### T CELLS

Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for a lung tumor protein. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the Isolex™ System, available from Nexell Therapeutics, Inc. Irvine, CA (see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a lung tumor polypeptide, polynucleotide encoding a lung tumor polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, a lung tumor polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a lung tumor polypeptide if the T cells specifically proliferate, secrete cytokines or kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell

proliferation can be detected by measuring an increased rate of DNA synthesis (*e.g.*, by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a lung tumor polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (*e.g.*, TNF or IFN-γ) is indicative of T cell activation (*see* Coligan et al., Current Protocols in Immunology, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a lung tumor polypeptide, polynucleotide or polypeptide-expressing APC may be CD4<sup>+</sup> and/or CD8<sup>+</sup>. Lung tumor protein-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from either a patient or a related, or unrelated, donor and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4<sup>+</sup> or CD8<sup>+</sup> T cells that proliferate in response to a lung tumor polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a lung tumor polypeptide, or a short peptide corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a lung tumor polypeptide. Alternatively, one or more T cells that proliferate in the presence of a lung tumor protein can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

25

#### PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides, T cells and/or binding agents disclosed herein may be incorporated into pharmaceutical compositions or immunogenic compositions (*i.e.*, vaccines). Pharmaceutical compositions comprise one or more such compounds and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds and an immunostimulant. An immunostimulant

30

may be any substance that enhances or potentiates an immune response to an exogenous antigen. Examples of immunostimulants include adjuvants, biodegradable microspheres (*e.g.*, polylactic galactide) and liposomes (into which the compound is incorporated; *see e.g.*, Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the composition or vaccine.

A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression systems. Numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope. In a preferred embodiment, the DNA may be introduced using a viral expression system (*e.g.*, vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler et al., *Proc. Natl.*

*Acad. Sci. USA* 90:11498-11502, 1993; Guzman et al., *Circulation* 88:2838-2848, 1993; and Guzman et al., *Cir. Res.* 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., *Science* 5 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier 10 will vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. 15 For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres 20 are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

Such compositions may also comprise buffers (e.g., neutral buffered saline or phosphate buffered saline), carbohydrates (e.g., glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA or glutathione, adjuvants (e.g., aluminum hydroxide) 25 and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of immunostimulants may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a 30 substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A,

*Bordetella pertussis* or *Mycobacterium tuberculosis* derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); AS-2 (SmithKline Beecham, Philadelphia, PA);  
5 aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

10                Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (*e.g.*, IFN- $\gamma$ , TNF $\alpha$ , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (*e.g.*, IL-4, IL-5, IL-6 and IL-10) tend to favor the  
15 induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using  
20 standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt.  
25 MPL adjuvants are available from Ribi ImmunoChem Research Inc. (Hamilton, MT) (*see* US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555 and WO 99/33488. Immunostimulatory DNA sequences  
30 are also described, for example, by Sato et al., *Science* 273:352, 1996. Another preferred adjuvant is a saponin, preferably QS21 (Aquila Biopharmaceuticals Inc.,

Framingham, MA), which may be used alone or in combination with other adjuvants. For example, an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with  
5 cholesterol, as described in WO 96/33739. Other preferred formulations comprises an oil-in-water emulsion and tocopherol. A particularly potent adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210.

Other preferred adjuvants include Montanide ISA 720 (Seppic, France),  
10 SAF (Chiron, California, United States), ISCOMS (CSL), MF-59 (Chiron), the SBAS series of adjuvants (*e.g.*, SBAS-2 or SBAS-4, available from SmithKline Beecham, Rixensart, Belgium), Detox (Ribi ImmunoChem Research Inc., Hamilton, MT), RC-529 (Ribi ImmunoChem Research Inc., Hamilton, MT) and Aminoalkyl glucosaminide 4-phosphates (AGPs).

15 Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient. The compositions described herein may be administered as part of a sustained release formulation (*i.e.*, a formulation such as a capsule, sponge or gel (composed of polysaccharides, for example) that effects a slow release of compound  
20 following administration). Such formulations may generally be prepared using well known technology (*see, e.g.* Coombes et al., *Vaccine* 14:1429-1438, 1996) and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix and/or contained  
25 within a reservoir surrounded by a rate controlling membrane.

Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. Such carriers include microparticles of poly(lactide-co-glycolide), as well as polyacrylate, latex, starch, cellulose and dextran. Other delayed-  
30 release carriers include supramolecular biovectors, which comprise a non-liquid hydrophilic core (*e.g.*, a cross-linked polysaccharide or oligosaccharide) and, optionally,

an external layer comprising an amphiphilic compound, such as a phospholipid (*see e.g.*, U.S. Patent No. 5,151,254 and PCT applications WO 94/20078, WO/94/23701 and WO 96/06638). The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy, *Ann. Rev. Med.* 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take up, process and present antigens with high efficiency, and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (*see* Zitvogel et al., *Nature Med.* 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood,

bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF $\alpha$  to cultures of monocytes  
5 harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF $\alpha$ , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

10 Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which  
15 correlates with the high expression of Fc $\gamma$  receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (e.g., CD54 and CD11) and costimulatory molecules (e.g., CD40, CD80, CD86 and 4-1BB).

20 APCs may generally be transfected with a polynucleotide encoding a lung tumor protein (or portion or other variant thereof) such that the lung tumor polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex vivo*, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein.  
25 Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell*  
30 *Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the lung tumor polypeptide, DNA



(naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (*e.g.*, vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (*e.g.*, a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of the polypeptide.

Vaccines and pharmaceutical compositions may be presented in unit-dose or multi-dose containers, such as sealed ampoules or vials. Such containers are preferably hermetically sealed to preserve sterility of the formulation until use. In general, formulations may be stored as suspensions, solutions or emulsions in oily or aqueous vehicles. Alternatively, a vaccine or pharmaceutical composition may be stored in a freeze-dried condition requiring only the addition of a sterile liquid carrier immediately prior to use.

#### 15 CANCER THERAPY

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as lung cancer. Within such methods, pharmaceutical compositions and vaccines are typically administered to a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. A cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor. Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides disclosed herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8<sup>+</sup> cytotoxic T lymphocytes and CD4<sup>+</sup> T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast and/or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies have shown that cultured effector cells can be induced to grow *in vivo* and to survive

long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (*see*, for example, Cheever et al., *Immunological Reviews* 157:177, 1997).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions disclosed herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g.*, intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (*i.e.*, untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25  $\mu$ g to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial, or longer disease-free

survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a lung tumor protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

#### METHODS FOR DETECTING CANCER

In general, a cancer may be detected in a patient based on the presence of one or more lung tumor proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, sputum urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as lung cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, a lung tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. *See, e.g.,* Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent

that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full length lung tumor proteins and portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10  $\mu$ g, and preferably about 100 ng to about 1  $\mu$ g, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the

binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.,* Pierce Immunotechnology Catalog and Handbook, 1991, at  
5 A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody.  
10 Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

15 More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to  
20 bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.,* incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with lung cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of  
25 that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

30 Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second

antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide.

5 An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are  
10 generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of  
15 the reaction products.

To determine the presence or absence of a cancer, such as lung cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average  
20 mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical*  
25 *Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (*i.e.*, the value that  
30 encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered

positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

5           In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution  
10           containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent.  
15           Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the  
20           biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1 $\mu$ g, and more preferably from about 50 ng to about  
25           500 ng. Such tests can typically be performed with a very small amount of biological sample.

          Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to  
30           those of ordinary skill in the art that the above protocols may be readily modified to use lung tumor polypeptides to detect antibodies that bind to such polypeptides in a



biological sample. The detection of such lung tumor protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a lung tumor protein in a biological sample. Within certain methods, a biological sample comprising CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient is incubated with a lung tumor polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with polypeptide (e.g., 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of lung tumor polypeptide to serve as a control. For CD4<sup>+</sup> T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8<sup>+</sup> T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a lung tumor protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a lung tumor cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (i.e., hybridizes to) a polynucleotide encoding the lung tumor protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a lung tumor protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%,

preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a lung tumor protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes will hybridize to a polynucleotide encoding a polypeptide disclosed herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a sequence recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349. Techniques for both PCR based assays and hybridization assays are well known in the art (*see*, for example, Mullis et al., *Cold Spring Harbor Symp. Quant. Biol.*, 51:263, 1987; Erlich ed., *PCR Technology*, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the disclosed compositions may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the

level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor.

- 5 One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

- As noted above, to improve sensitivity, multiple lung tumor protein  
10 markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins  
15 provided herein may be combined with assays for other known tumor antigens.

#### DIAGNOSTIC KITS

- The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components  
20 necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a lung tumor protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements,  
25 such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

- Alternatively, a kit may be designed to detect the level of mRNA encoding a lung tumor protein in a biological sample. Such kits generally comprise at  
30 least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a lung tumor protein. Such an oligonucleotide may be used,

for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a lung tumor protein.

The following Examples are offered by way of illustration and not by  
5 way of limitation.

EXAMPLE 1  
ISOLATION AND CHARACTERIZATION OF cDNA SEQUENCES  
ENCODING LUNG TUMOR POLYPEPTIDES

5

This example illustrates the isolation of cDNA molecules encoding lung tumor-specific polypeptides from lung tumor cDNA libraries.

A. ISOLATION OF cDNA SEQUENCES FROM A LUNG SQUAMOUS CELL  
10 CARCINOMA LIBRARY

A human lung squamous cell carcinoma cDNA expression library was constructed from poly A<sup>+</sup> RNA from a pool of two patient tissues using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies, Gaithersburg, MD) following the manufacturer's protocol. Specifically, lung carcinoma  
15 tissues were homogenized with polytron (Kinematica, Switzerland) and total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A<sup>+</sup> RNA was then purified using an oligo dT cellulose column as described in Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989. First-strand cDNA was  
20 synthesized using the NotI/Oligo-dT18 primer. Double-stranded cDNA was synthesized, ligated with BstXI/EcoRI adaptors (Invitrogen, San Diego, CA) and digested with NotI. Following size fractionation with cDNA size fractionation columns (BRL Life Technologies), the cDNA was ligated into the BstXI/NotI site of pcDNA3.1 (Invitrogen) and transformed into ElectroMax *E. coli* DH10B cells (BRL Life  
25 Technologies) by electroporation.

Using the same procedure, a normal human lung cDNA expression library was prepared from a pool of four tissue specimens. The cDNA libraries were characterized by determining the number of independent colonies, the percentage of clones that carried insert, the average insert size and by sequence analysis. The lung  
30 squamous cell carcinoma library contained  $2.7 \times 10^6$  independent colonies, with 100% of clones having an insert and the average insert size being 2100 base pairs. The normal

lung cDNA library contained  $1.4 \times 10^6$  independent colonies, with 90% of clones having inserts and the average insert size being 1800 base pairs. For both libraries, sequence analysis showed that the majority of clones had a full length cDNA sequence and were synthesized from mRNA

5 cDNA library subtraction was performed using the above lung squamous cell carcinoma and normal lung cDNA libraries, as described by Hara *et al.* (*Blood*, 84:189-199, 1994) with some modifications. Specifically, a lung squamous cell carcinoma-specific subtracted cDNA library was generated as follows. Normal tissue cDNA library (80  $\mu$ g) was digested with BamHI and XhoI, followed by a filling-in  
10 reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol precipitation, the DNA was dissolved in 133  $\mu$ l of H<sub>2</sub>O, heat-denatured and mixed with 133  $\mu$ l (133  $\mu$ g) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (67  $\mu$ l) was added  
15 and the biotinylation reaction was repeated. After extraction with butanol five times, the DNA was ethanol-precipitated and dissolved in 23  $\mu$ l H<sub>2</sub>O to form the driver DNA.

To form the tracer DNA, 10  $\mu$ g lung squamous cell carcinoma cDNA library was digested with NotI and SpeI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech, Palo Alto, CA). Typically, 5  $\mu$ g of  
20 cDNA was recovered after the sizing column. Following ethanol precipitation, the tracer DNA was dissolved in 5  $\mu$ l H<sub>2</sub>O. Tracer DNA was mixed with 15  $\mu$ l driver DNA and 20  $\mu$ l of 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and  
25 incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three more times. Subtracted DNA was precipitated, dissolved in 12  $\mu$ l H<sub>2</sub>O, mixed with 8  $\mu$ l driver DNA and 20  $\mu$ l of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After  
30 removal of biotinylated double-stranded DNA, subtracted cDNA was ligated into NotI/SpeI site of chloramphenicol resistant pBCSK<sup>+</sup> (Stratagene, La Jolla, CA) and

transformed into ElectroMax *E. coli* DH10B cells by electroporation to generate a lung squamous cell carcinoma specific subtracted cDNA library (herein after referred to as "lung subtraction I").

A second lung squamous cell carcinoma specific subtracted cDNA library (referred to as "lung subtraction II") was generated in a similar way to the lung subtraction library I, except that eight frequently recovered genes from lung subtraction I were included in the driver DNA, and 24,000 independent clones were recovered.

To analyze the subtracted cDNA libraries, plasmid DNA was prepared from 320 independent clones, randomly picked from the subtracted lung squamous cell carcinoma specific libraries. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A and/or Model 377 (Foster City, CA). The cDNA sequences for sixty isolated clones are provided in SEQ ID NO: 1-60. These sequences were compared to known sequences in the gene bank using the EMBL and GenBank databases (release 96). No significant homologies were found to the sequences provided in SEQ ID NO: 2, 3, 19, 38 and 46. The sequences of SEQ ID NO: 1, 6-8, 10-13, 15, 17, 18, 20-27, 29, 30, 32, 34-37, 39-45, 47-49, 51, 52, 54, 55 and 57-59 were found to show some homology to previously identified expressed sequence tags (ESTs). The sequences of SEQ ID NO: 9, 28, 31 and 33 were found to show some homology to previously identified non-human gene sequences and the sequences of SEQ ID NO: 4, 5, 14, 50, 53, 56 and 60 were found to show some homology to gene sequences previously identified in humans.

The subtraction procedure described above was repeated using the above lung squamous cell carcinoma cDNA library as the tracer DNA, and the above normal lung tissue cDNA library and a cDNA library from normal liver and heart (constructed from a pool of one sample of each tissue as described above), plus twenty other cDNA clones that were frequently recovered in lung subtractions I and II, as the driver DNA (lung subtraction III). The normal liver and heart cDNA library contained  $1.76 \times 10^6$  independent colonies, with 100% of clones having inserts and the average insert size being 1600 base pairs. Ten additional clones were isolated (SEQ ID NO: 61-70). Comparison of these cDNA sequences with those in the gene bank as described above,

revealed no significant homologies to the sequences provided in SEQ ID NO: 62 and 67. The sequences of SEQ ID NO: 61, 63-66, 68 and 69 were found to show some homology to previously isolated ESTs and the sequence provided in SEQ ID NO: 70 was found to show some homology to a previously identified rat gene.

5 In further studies, the subtraction procedure described above was repeated using the above lung squamous cell carcinoma cDNA library as the tracer DNA, and a cDNA library from a pool of normal lung, kidney, colon, pancreas, brain, resting PBMC, heart, skin and esophagus as the driver DNA, with esophagus cDNAs making up one third of the driver material. Since esophagus is enriched in normal  
10 epithelial cells, including differentiated squamous cells, this procedure is likely to enrich genes that are tumor specific rather than tissues specific. The cDNA sequences of 48 clones determined in this subtraction are provided in SEQ ID NO: 177-224. The sequences of SEQ ID NO: 177, 178, 180, 181, 183, 187, 192, 195-197, 208, 211, 212, 215, 216, 218 and 219 showed some homology to previously identified genes. The  
15 sequences of SEQ ID NO: 179, 182, 184-186, 188-191, 193, 194, 198-207, 209 210, 213, 214, 217, 220 and 224 showed some homology to previously determined ESTs. The sequence of SEQ ID NO: 221-223 showed no homology to any previously determined sequence.

## 20 B. ISOLATION OF cDNA SEQUENCES FROM A LUNG ADENOCARCINOMA LIBRARY

A human lung adenocarcinoma cDNA expression library was constructed as described above. The library contained  $3.2 \times 10^6$  independent colonies, with 100% of clones having an insert and the average insert size being 1500 base pairs.  
25 Library subtraction was performed as described above using the normal lung and normal liver and heart cDNA expression libraries described above as the driver DNA. Twenty-six hundred independent clones were recovered.

Initial cDNA sequence analysis from 100 independent clones revealed many ribosomal protein genes. The cDNA sequences for fifteen clones isolated in this  
30 subtraction are provided in SEQ ID NO: 71-86. Comparison of these sequences with those in the gene bank as described above revealed no significant homologies to the



sequence provided in SEQ ID NO: 84. The sequences of SEQ ID NO: 71, 73, 74, 77, 78 and 80-82 were found to show some homology to previously isolated ESTs, and the sequences of SEQ ID NO: 72, 75, 76, 79, 83 and 85 were found to show some homology to previously identified human genes.

5 In further studies, a cDNA library (referred to as mets3616A) was constructed from a metastatic lung adenocarcinoma. The determined cDNA sequences of 25 clones sequenced at random from this library are provided in SEQ ID NO: 255-279. The mets3616A cDNA library was subtracted against a cDNA library prepared from a pool of normal lung, liver, pancreas, skin, kidney, brain and resting PBMC. To  
10 increase the specificity of the subtraction, the driver was spiked with genes that were determined to be most abundant in the mets3616A cDNA library, such as EF1-alpha, integrin-beta and anticoagulant protein PP4, as well as with cDNAs that were previously found to be differentially expressed in subtracted lung adenocarcinoma cDNA libraries. The determined cDNA sequences of 51 clones isolated from the  
15 subtracted library (referred to as mets3616A-S1) are provided in SEQ ID NO: 280-330.

Comparison of the sequences of SEQ ID NO: 255-330 with those in the public databases revealed no significant homologies to the sequences of SEQ ID NO: 255-258, 260, 262-264, 270, 272, 275, 276, 279, 281, 287, 291, 296, 300 and 310. The sequences of SEQ ID NO: 259, 261, 265-269, 271, 273, 274, 277, 278, 282-285, 288-  
20 290, 292, 294, 297-299, 301, 303-309, 313, 314, 316, 320-324 and 326-330 showed some homology to previously identified gene sequences, while the sequences of SEQ ID NO: 280, 286, 293, 302, 310, 312, 315, 317-319 and 325 showed some homology to previously isolated expressed sequence tags (ESTs).

25

## EXAMPLE 2

### DETERMINATION OF TISSUE SPECIFICITY OF LUNG TUMOR POLYPEPTIDES

Using gene specific primers, mRNA expression levels for seven  
30 representative lung tumor polypeptides described in Example 1 were examined in a variety of normal and tumor tissues using RT-PCR.

Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent as described above. First strand synthesis was carried out using 2 µg of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 °C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR, β-actin was used as an internal control for each of the tissues examined. 1 µl of 1:30 dilution of cDNA was employed to enable the linear range amplification of the β-actin template and was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the β-actin levels were determined for each reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

mRNA Expression levels were examined in five different types of tumor tissue (lung squamous cell carcinoma from 3 patients, lung adenocarcinoma, colon tumor from 2 patients, breast tumor and prostate tumor), and thirteen different normal tissues (lung from 4 donors, prostate, brain, kidney, liver, ovary, skeletal muscle, skin, small intestine, stomach, myocardium, retina and testes). Using a 10-fold amount of cDNA, the antigen LST-S1-90 (SEQ ID NO: 3) was found to be expressed at high levels in lung squamous cell carcinoma and in breast tumor, and at low to undetectable levels in the other tissues examined.

The antigen LST-S2-68 (SEQ ID NO: 15) appears to be specific to lung and breast tumor, however, expression was also detected in normal kidney. Antigens LST-S1-169 (SEQ ID NO: 6) and LST-S1-133 (SEQ ID NO: 5) appear to be very abundant in lung tissues (both normal and tumor), with the expression of these two genes being decreased in most of the normal tissues tested. Both LST-S1-169 and LST-S1-133 were also expressed in breast and colon tumors. Antigens LST-S1-6 (SEQ ID NO: 7) and LST-S2-I2-5F (SEQ ID NO: 47) did not show tumor or tissue specific expression, with the expression of LST-S1-28 being rare and only detectable in a few tissues. The antigen LST-S3-7 (SEQ ID NO: 63) showed lung and breast tumor specific expression, with its message only being detected in normal testes when the PCR was performed for 30 cycles. Lower level expression was detected in some

normal tissues when the cycle number was increased to 35. Antigen LST-S3-13 (SEQ ID NO: 66) was found to be expressed in 3 out of 4 lung tumors, one breast tumor and both colon tumor samples. Its expression in normal tissues was lower compared to tumors, and was only detected in 1 out of 4 normal lung tissues and in normal tissues  
5 from kidney, ovary and retina. Expression of antigens LST-S3-4 (SEQ ID NO: 62) and LST-S3-14 (SEQ ID NO: 67) was rare and did not show any tissue or tumor specificity. Consistent with Northern blot analyses, the RT-PCT results on antigen LAT-S1-A-10A (SEQ ID NO: 78) suggested that its expression is high in lung, colon, stomach and small intestine tissues, including lung and colon tumors, whereas its expression was low  
10 or undetectable in other tissues.

A total of 2002 cDNA fragments isolated in lung subtractions I, II and III, described above, were colony PCR amplified and their mRNA expression levels in lung tumor, normal lung, and various other normal and tumor tissues were determined using microarray technology (Synteni, Palo Alto, CA). Briefly, the PCR amplification  
15 products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization  
20 intensity. Seventeen non-redundant cDNA clones showed over-expression in lung squamous tumors, with expression in normal tissues tested (lung, skin, lymph node, colon, liver, pancreas, breast, heart, bone marrow, large intestine, kidney, stomach, brain, small intestine, bladder and salivary gland) being either undetectable, or 10-fold less compared to lung squamous tumors. The determined partial cDNA sequences for  
25 the clone L513S are provided in SEQ ID NO: 87 and 88; those for L514S are provided in SEQ ID NO: 89 and 90; those for L516S in SEQ ID NO: 91 and 92; that for L517S in SEQ ID NO: 93; that for L519S in SEQ ID NO: 94; those for L520S in SEQ ID NO: 95 and 96; those for L521S in SEQ ID NO: 97 and 98; that for L522S in SEQ ID NO: 99; that for L523S in SEQ ID NO: 100; that for L524S in SEQ ID NO: 101; that for  
30 L525S in SEQ ID NO: 102; that for L526S in SEQ ID NO: 103; that for L527S in SEQ ID NO: 104; that for L528S in SEQ ID NO: 105; that for L529S in SEQ ID NO: 106;

and those for L530S in SEQ ID NO: 107 and 108. Additionally, the full-length cDNA sequence for L530S is provided in SEQ ID NO: 151, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 152. L530S shows homology to a splice variant of a p53 tumor suppressor homologue, p63. The cDNA sequences of 7 known isoforms of p63 are provided in SEQ ID NO: 331-337, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 338-344, respectively.

Due to polymorphisms, the clone L531S appears to have two forms. A first determined full-length cDNA sequence for L531S is provided in SEQ ID NO: 109, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 110. A second determined full-length cDNA sequence for L531S is provided in SEQ ID NO: 111, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 112. The sequence of SEQ ID NO: 111 is identical to that of SEQ ID NO: 109, except that it contains a 27 bp insertion. Similarly, L514S also has two alternatively spliced forms; the first variant cDNA is listed as SEQ ID NO: 153, with the corresponding amino acid sequence being provided in SEQ ID NO: 155. The second variant form of L514S full-length cDNA is provided in SEQ ID NO: 154, with its corresponding amino acid sequence being provided in SEQ ID NO: 156.

Full length cloning for L524S (SEQ ID NO: 101) yielded two variants (SEQ ID NO: 163 and 164) with the corresponding predicted amino acid sequences of SEQ ID NO: 165 and 166, respectively. Both variants have been shown to encode parathyroid hormone-related peptide.

Attempts to isolate the full-length cDNA for L519S, resulted in the isolation of the extended cDNA sequence provided in SEQ ID NO: 173, which contains a potential open reading frame. The predicted amino acid sequence encoded by the sequence of SEQ ID NO: 173 is provided in SEQ ID NO: 174. Additionally, the full-length cDNA sequence for the clone of SEQ ID NO: 100 (known as L523S), a known gene, is provided in SEQ ID NO: 175, with the corresponding predicted amino acid sequence provided in SEQ ID NO: 176. In further studies, a full-length cDNA sequence for L523S was isolated from a L523S-positive tumor cDNA library by PCR amplification using gene specific primers designed from the sequence of SEQ ID NO: 175. The determined cDNA sequence is provided in SEQ ID NO: \*\*. The amino acid

sequence encoded by this sequence is provided in SEQ ID NO: \*\*. This protein sequence differs from the previously published protein sequence at two amino acid positions, namely at positions 158 and 410.

Comparison of the sequences of L514S and L531S (SEQ ID NO: 87 and 88, 89 and 90, and 109, respectively) with those in the gene bank, as described above, revealed no significant homologies to known sequences. The sequences of L513S, L516S, L517S, L519S, L520S and L530S (SEQ ID NO: 87 and 88, 91 and 92, 93, 94, 95 and 96, 107 and 108, respectively) were found to show some homology to previously identified ESTs. The sequences of L521S, L522S, L523S, L524S, L525S, L526S, L527S, L528S and L529S (SEQ ID NO: 97 and 98, 99, 99, 101, 102, 103, 104, 105, and 106, respectively) were found to represent known genes. The determined full-length cDNA sequences for L520S is provided in SEQ ID NO: 113, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 114. Subsequent microarray analysis has shown L520S to be overexpressed in breast tumors in addition to lung squamous tumors.

Further analysis has demonstrated that L529S (SEQ ID NO: 106 and 115), L525S (SEQ ID NO: 102 and 120) and L527S (SEQ ID NO: 104) are cytoskeletal components and potentially squamous cell specific proteins. L529S is connexin 26, a gap junction protein. It is highly expressed in lung squamous tumor 9688T, and moderately over-expressed in two others. However, lower level expression of connexin 26 is also detectable in normal skin, colon, liver and stomach. The over-expression of connexin 26 in some breast tumors has been reported and a mutated form of L529S may result in over-expression in lung tumors. L525S is plakophilin 1, a desmosomal protein found in plaque-bearing adhering junctions of the skin. Expression levels for L525S mRNA is highly elevated in three out of four lung squamous tumors tested, and in normal skin. L527S has been identified as keratin 6 isoform, type II 58 Kd keratin, and cytokeratin 13 and shows over-expression in squamous tumors and low expression in normal skin, breast and colon tissues. Notably, keratin and keratin-related genes have been extensively documented as potential markers for lung cancer including CYFRA2.1 (Pastor, A., et al, *Eur. Respir. J.*, 10:603-609, 1997). L513S (SEQ ID NO: 87 and 88)

shows moderate over-expression in several tumor tissues tested, and encodes a protein that was first isolated as a pemphigus vulgaris antigen.

L520S (SEQ ID NO: 95 and 96) and L521S (SEQ ID NO: 97 and 98) are highly expressed in lung squamous tumors, and L520S is up-regulated in normal salivary gland and L521S is over-expressed in normal skin. Both belong to a family of small proline rich proteins and represent markers for fully differentiated squamous cells. L521S has been described as a specific marker for lung squamous tumor (Hu, R., et al, *Lung Cancer*, 20:25-30, 1998). L515S (SEQ ID NO: 162) encodes IGF- $\beta$ 2 and L516S is an aldose reductase homologue and both are moderately expressed in lung squamous tumors and in normal colon. Notably, L516S (SEQ ID NO: 91 and 92) is up-regulated in metastatic tumors but not primary lung adenocarcinoma, an indication of its potential role in metatasis and a potential prognostic marker. L522S (SEQ ID NO: 99) is moderately over-expressed in lung squamous tumors with minimum expression in normal tissues. L522S has been shown to belong to a class IV alcohol dehydrogenase, ADH7, and its expression profile suggests it is a squamous cell specific antigen. L523S (SEQ ID NO: 100) is moderately over-expressed in lung squamous tumor, human pancreatic cancer cell lines and pancreatic cancer tissues, suggesting this gene may be a shared antigen between pancreatic and lung squamous cell cancer.

L524S (SEQ ID NO: 101) is over-expressed in the majority of squamous tumors tested and is homologous with parathyroid hormone-related peptide (PTHrP), which is best known to cause humoral hypercalcaemia associated with malignant tumors such as leukemia, prostate and breast cancer. It is also believed that PTHrP is most commonly associated with squamous carcinoma of lung and rarely with lung adenocarcinoma (Davidson, L.A., et al, *J. Pathol.*, 178: 398-401, 1996). L528S (SEQ ID NO: 105) is highly over-expressed in two lung squamous tumors with moderate expression in two other squamous tumors, one lung adenocarcinoma and some normal tissues, including skin, lymph nodes, heart, stomach and lung. It encodes the NMB gene that is similar to the precursor of melanocyte specific gene Pmel17, wfhich is reported to be preferentially expressed in low-metastatic potential melanoma cell lines. This suggests that L528S may be a shared antigen in both melanoma and lung squamous cell carcinoma. L526S (SEQ ID NO: 103) is overexpressed in all lung

squamous cell tumor tissues tested and has been shown to share homology with a gene (ATM) in which a mutation causes ataxia telangiectasia, a genetic disorder in humans causing a predisposition to cancer, among other symptoms. ATM encodes a protein that activates p53 mediated cell-cycle checkpoint through direct binding and phosphorylation of the p53 molecule. Approximately 40% of lung cancer is associated with p53 mutations, and it is speculated that over-expression of ATM is a result of compensation for loss of p53 function, but it is unknown whether over-expression is the cause of result of lung squamous cell carcinoma. Additionally, expression of L526S (ATM) is also detected in a metastatic but not lung adenocarcinoma, suggesting a role in metastasis.

Expression of L523S (SEQ ID NO: 175), was also examined by real time RT-PCR as described above. In a first study using a panel of lung squamous tumors, L523S was found to be expressed in 4/7 lung squamous tumors, 2/3 head and neck squamous tumors and 2/2 lung adenocarcinomas, with low level expression being observed in skeletal muscle, soft palate and tonsil. In a second study using a lung adenocarcinoma panel, expression of L523S was observed in 4/9 primary adenocarcinomas, 2/2 lung pleural effusions, 1/1 metastatic lung adenocarcinomas and 2/2 lung squamous tumors, with little expression being observed in normal tissues.

Expression of L523S in lung tumors and various normal tissues was also examined by Northern blot analysis, using standard techniques. In a first study, L523S was found to be expressed in a number of lung adenocarcinomas and squamous cell carcinomas, as well as normal tonsil. No expression was observed in normal lung. In a second study using a normal tissue blot (HB-12) from Clontech, no expression was observed in brain, skeletal muscle, colon, thymus, spleen, kidney, liver, small intestine, lung or PBMC, although there was strong expression in placenta.

### EXAMPLE 3

#### ISOLATION AND CHARACTERIZATION OF LUNG TUMOR POLYPEPTIDES BY PCR-BASED SUBTRACTION

Eight hundred and fifty seven clones from a cDNA subtraction library, containing cDNA from a pool of two human lung squamous tumors subtracted against eight normal human tissue cDNAs including lung, PBMC, brain, heart, kidney, liver, pancreas, and skin, (Clontech, Palo Alto, CA) were derived and submitted to a first  
5 round of PCR amplification. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The resulting cDNA fragments were subcloned into the vector P7- Adv vector (Clontech, Palo Alto, CA) and transformed into DH5 $\alpha$  *E. coli* (Gibco, BRL). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated  
10 Sequencer Model 373A.

One hundred and sixty two positive clones were sequenced. Comparison of the DNA sequences of these clones with those in the the EMBL and GenBank databases, as described above, revealed no significant homologies to 13 of these clones, hereinafter referred to as Contigs 13, 16, 17, 19, 22, 24, 29, 47, 49, 56-59. The  
15 determined cDNA sequences for these clones are provided in SEQ ID NO: 125, 127-129, 131-133, 142, 144, 148-150, and 157, respectively. Contigs 1, 3-5, 7-10, 12, 11, 15, 20, 31, 33, 38, 39, 41, 43, 44, 45, 48, 50, 53, 54 (SEQ ID NO: 115-124, 126, 130, 134-141, 143, 145-147, respectively) were found to show some degree of homology to previously identified DNA sequences. Contig 57 (SEQ ID NO: 149) was found to  
20 represent the clone L519S (SEQ ID NO: 94) disclosed in US. Patent Application No. 09/123,912, filed July 27, 1998. To the best of the inventors' knowledge, none of these sequences have been previously shown to be differentially over-expressed in lung tumors.

mRNA expression levels for representative clones in lung tumor tissues,  
25 normal lung tissues (n=4), resting PBMC, salivary gland, heart, stomach, lymph nodes, skeletal muscle, soft palate, small intestine, large intestine, bronchial, bladder, tonsil, kidney, esophagus, bone marrow, colon, adrenal gland, pancreas, and skin, (all derived from human) were determined by RT-PCR as described above. Expression levels using microarray technology, as described above, were examined in one sample of each tissue  
30 type unless otherwise indicated.



Contig 3 (SEQ ID NO: 116) was found to be highly expressed in all head and neck squamous cell tumors tested (17/17), and expressed in the majority (8/12) of lung squamous tumors, (high expression in 7/12, moderate in 2/12, and low in 2/12), while showing negative expression for 2/4 normal lung tissues and low expression in the remaining two samples. Contig 3 showed moderate expression in skin and soft palate, and lowered expression levels in resting PBMC, large intestine, salivary gland, tonsil, pancreas, esophagus, and colon. Contig 11 (SEQ ID NO: 124) was found to be expressed in all head and neck squamous cell tumors tested (17/17): highly expressed in 14/17, and moderately expressed in 3/17. Additionally, expression in lung squamous tumors showed high expression in 3/12 and moderate in 4/12. Contig 11 was negative for 3/4 normal lung samples, with the remaining sample having only low expression. Contig 11 showed low to moderate reactivity to salivary gland, soft palate, bladder, tonsil, skin, esophagus, and large intestine. Contig 13 (SEQ ID NO: 125) was found to be expressed in all head and neck squamous cell tumors tested (17/17): highly expressed in 12/17, and moderately expressed in 5/17. Contig 13 was expressed in 7/12 lung squamous tumors, with high expression in 4/12 and moderate expression in three samples. Analysis of normal lung samples showed negative expression for 2/4 and low to moderate expression in the remaining two samples. Contig 13 did show low to moderate reactivity to resting PBMC, salivary gland, bladder, pancreas, tonsil, skin, esophagus, and large intestine, as well as high expression in soft palate. Contig 16 (SEQ ID NO: 127) was found to be moderately expressed in some head and neck squamous cell tumors (6/17) and one lung squamous tumor; while showing no expression in any normal lung samples tested. Contig 16 did show low reactivity to resting PBMC, large intestine, skin, salivary gland, and soft palate. Contig 17 (SEQ ID NO: 128) was shown to be expressed in all head and neck squamous cell tumors tested (17/17): highly expressed in 5/17, and moderately expressed in 12/17. Expression levels in lung squamous tumors showed one tumor sample with high expression and 3/12 with moderate levels. Contig 17 was negative for 2/4 normal lung samples, with the remaining samples having only low expression. Additionally, low level expression was found in esophagus and soft palate. Contig 19 (SEQ ID NO: 129) was found to be expressed in most head and neck squamous cell tumors tested (11/17); with two

samples having high levels, 6/17 showing moderate expression, and low expression being found in 3/17. Testing in lung squamous tumors revealed only moderate expression in 3/12 samples. Expression levels in 2/4 of normal lung samples were negative, the two other samples having only low expression. Contig 19 showed low expression levels in esophagus, resting PBMC, salivary gland, bladder, soft palate and pancreas.

Contig 22 (SEQ ID NO: 131), was shown to be expressed in most head and neck squamous cell tumors tested (13/17) with high expression in four of these samples, moderate expression in 6/17, and low expression in 3/17. Expression levels in lung squamous tumors were found to be moderate to high for 3/12 tissues tested, with negative expression in two normal lung samples and low expression in two other samples (n=4). Contig 22 showed low expression in skin, salivary gland and soft palate. Similarly, Contig 24 (SEQ ID NO: 132) was found to be expressed in most head and neck squamous cell tumors tested (13/17) with high expression in three of these samples, moderate expression in 6/17, and low expression in 4/17. Expression levels in lung squamous tumors were found to be moderate to high for 3/12 tissues tested, with negative expression for three normal lung samples and low expression in one sample (n=4). Contig 24 showed low expression in skin, salivary gland and soft palate. Contig 29 (SEQ ID NO: 133) was expressed in nearly all head and neck squamous cell tumors tested (16/17): highly expressed in 4/17, moderately expressed in 11/17, with low expression in one sample. Also, it was moderately expressed in 3/12 lung squamous tumors, while being negative for 2/4 normal lung samples. Contig 29 showed low to moderate expression in large intestine, skin, salivary gland, pancreas, tonsil, heart and soft palate. Contig 47 (SEQ ID NO: 142) was expressed in most head and neck squamous cell tumors tested (12/17): moderate expression in 10/17, and low expression in two samples. In lung squamous tumors, it was highly expressed in one sample and moderately expressed in two others (n=13). Contig 47 was negative for 2/4 normal lung samples, with the remaining two samples having moderate expression. Also, Contig 47 showed moderate expression in large intestine, and pancreas, and low expression in skin, salivary gland, soft palate, stomach, bladder, resting PBMC, and tonsil.

Contig 48 (SEQ ID NO: 143) was expressed in all head and neck squamous cell tumors tested (17/17): highly expressed in 8/17 and moderately expressed in 7/17, with low expression in two samples. Expression levels in lung squamous tumors were high to moderate in three samples (n=13). Contig 48 was  
5 negative for one out of four normal lung samples, the remaining showing low or moderate expression. Contig 48 showed moderate expression in soft palate, large intestine, pancreas, and bladder, and low expression in esophagus, salivary gland, resting PBMC, and heart. Contig 49 (SEQ ID NO: 144) was expressed at low to moderate levels in 6/17 head and neck squamous cell tumors tested. Expression levels  
10 in lung squamous tumors were moderate in three samples (n=13). Contig 49 was negative for 2/4 normal lung samples, the remaining samples showing low expression. Moderate expression levels in skin, salivary gland, large intestine, pancreas, bladder and resting PBMC were shown, as well as low expression in soft palate, lymph nodes, and tonsil. Contig 56 (SEQ ID NO: 148) was expressed in low to moderate levels in 3/17  
15 head and neck squamous cell tumors tested, and in lung squamous tumors, showing low to moderate levels in three out of thirteen samples. Notably, low expression levels were detected in one adenocarcinoma lung tumor sample (n=2). Contig 56 was negative for 3/4 normal lung samples, and showed moderate expression levels in only large intestine, and low expression in salivary gland, soft palate, pancreas, bladder, and  
20 resting PBMC. Contig 58, also known as L769P, (SEQ ID NO: 150) was expressed at moderate levels in 11/17 head and neck squamous cell tumors tested and low expression in one additional sample. Expression in lung squamous tumors showed low to moderate levels in three out of thirteen samples. Contig 58 was negative for 3/4 normal lung samples, with one sample having low expression. Moderate expression levels in  
25 skin, large intestine, and resting PBMC were demonstrated, as well as low expression in salivary gland, soft palate, pancreas, and bladder. Contig 59 (SEQ ID NO: 157) was expressed in some head, neck, and lung squamous tumors. Low level expression of Contig 59 was also detected in salivary gland and large intestine.

The full-length cDNA sequence for Contig 22, also referred to as L763P,  
30 is provided in SEQ ID NO: 158, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 159. Real-time RT-PCR analysis of L763P revealed

that it is highly expressed in 3/4 lung squamous tumors as well as 4/4 head and neck squamous tumors, with low level expression being observed in normal brain, skin, soft pallet and trachea. Subsequent database searches revealed that the sequence of SEQ ID NO: 158 contains a mutation, resulting in a frameshift in the corresponding protein sequence. A second cDNA sequence for L763P is provided in SEQ ID NO: 345, with the corresponding amino acid sequence being provided in SEQ ID NO: 346. The sequences of SEQ ID NO: 159 and 346 are identical with the exception of the C-terminal 33 amino acids of SEQ ID NO: 159.

The full-length cDNA sequence incorporating Contigs 17, 19, and 24, referred to as L762P, is provided in SEQ ID NO: 160, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 161. Further analysis of L762P has determined it to be a type I membrane protein and two additional variants have been sequenced. Variant 1 (SEQ ID NO: 167, with the corresponding amino acid sequence in SEQ ID NO: 169) is an alternatively spliced form of SEQ ID NO: 160 resulting in deletion of 503 nucleotides, as well as deletion of a short segment of the expressed protein. Variant 2 (SEQ ID NO: 168, with the corresponding amino acid sequence in SEQ ID NO: 170) has a two nucleotide deletion at the 3' coding region in comparison to SEQ ID NO: 160, resulting in a secreted form of the expressed protein. Real-time RT-PCR analysis of L762P revealed that is over-expressed in 3/4 lung squamous tumors and 4/4 head & neck tumors, with low level expression being observed in normal skin, soft pallet and trachea.

The full-length cDNA sequence for contig 56 (SEQ ID NO: 148), also referred to as L773P, is provided in SEQ ID NO: 171, with the predicted amino acid sequence in SEQ ID NO: 172. L773P was found to be identical to dihydroxyl dehydrogenase at the 3' portion of the gene, with divergent 5' sequence. As a result, the 69 N-terminal amino acids are unique. The cDNA sequence encoding the 69 N-terminal amino acids is provided in SEQ ID NO: 349, with the N-terminal amino acid sequence being provided in SEQ ID NO: 350. Real-time PCR revealed that L773P is highly expressed in lung squamous tumor and lung adenocarcinoma, with no detectable expression in normal tissues. Subsequent Northern blot analysis of L773P demonstrated that this transcript is differentially over-expressed in squamous tumors

and detected at approximately 1.6 Kb in primary lung tumor tissue and approximately 1.3 Kb in primary head and neck tumor tissue.

Subsequent microarray analysis has shown Contig 58, also referred to as L769S (SEQ ID NO: 150), to be overexpressed in breast tumors in addition to lung squamous tumors.

#### EXAMPLE 4

##### SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems Division 430A peptide synthesizer using Fmoc chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

#### EXAMPLE 5

##### PREPARATION OF ANTIBODIES AGAINST LUNG CANCER ANTIGENS

Polyclonal antibodies against the lung cancer antigens L514S, L528S and L531S (SEQ ID NO: 155, 225 and 112, respectively) were prepared as follows.

Rabbits were immunized with recombinant protein expressed in and purified from *E. coli* as described above. For the initial immunization, 400 µg of

antigen combined with muramyl dipeptide (MDP) was injected subcutaneously (S.C.). Animals were boosted S.C. 4 weeks later with 200 µg of antigen mixed with incomplete Freund's Adjuvant (IFA). Subsequent boosts of 100 µg of antigen mixed with IFA were injected S.C. as necessary to induce high antibody titer responses. Serum bleeds  
5 from immunized rabbits were tested for antigen-specific reactivity using ELISA assays with purified protein. Polyclonal antibodies against L514S, L528S and L531S were affinity purified from high titer polyclonal sera using purified protein attached to a solid support.

Immunohistochemical analysis using polyclonal antibodies against  
10 L514S was performed on a panel of 5 lung tumor samples, 5 normal lung tissue samples and normal colon, kidney, liver, brain and bone marrow. Specifically, tissue samples were fixed in formalin solution for 24 hours and embedded in paraffin before being sliced into 10 micron sections. Tissue sections were permeabilized and incubated with antibody for 1 hr. HRP-labeled anti-mouse followed by incubation with DAB  
15 chromogen was used to visualize L514S immunoreactivity. L514S was found to be highly expressed in lung tumor tissue with little or no expression being observed in normal lung, brain or bone marrow. Light staining was observed in colon and kidney. Staining was seen in normal liver but no mRNA has been detected in this tissue making this result suspect.

20

## EXAMPLE 6

### PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

Immunogenic peptides from the lung cancer antigen L762P (SEQ ID  
25 NO: 161) for HLA-A2/K<sup>b</sup>-restricted CD8<sup>+</sup> T cells were identified as follows.

The location of HLA-A2 binding peptides within the lung cancer antigen L762P (SEQ ID NO: 161) was predicted using a computer program which predicts peptides sequences likely to being to HLA-A\*0201 by fitting to the known peptide binding motif for HLA-A\*0201 (Rupert *et al.* (1993) *Cell* 74:929; Rammensee *et al.*  
30 (1995) *Immunogenetics* 41:178-228). A series of 19 synthetic peptides corresponding to a selected subset of the predicted HLA-A\*0201 binding peptides was prepared as described above.

Mice expressing the transgene for human HLA A2/K<sup>b</sup> (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with the synthetic peptides, as described by Theobald et al., *Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995 with the following modifications. Mice were immunized with 50µg of L726P peptide and 120µg of an I-A<sup>b</sup> binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single cell suspensions prepared. Cells were then resuspended at  $7 \times 10^6$  cells/ml in complete media (RPMI-1640; Gibco BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium pyruvate (Gibco BRL), non-essential amino acids (Gibco BRL),  $2 \times 10^{-5}$  M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) L762P peptide- (5µg/ml) and 10mg/ml B<sub>2</sub>-microglobulin- (3 µg/ml) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). After six days, cells ( $5 \times 10^5$ /ml) were restimulated with  $2.5 \times 10^6$ /ml peptide pulsed irradiated (20,000 rads) EL4A2Kb cells (Sherman et al, *Science* 258:815-818, 1992) and  $5 \times 10^6$ /ml irradiated (3000 rads) A2/K<sup>b</sup>-transgenic spleen feeder cells. Cells were cultured in the presence of 10U/ml IL-2. Cells were restimulated on a weekly basis as described, in preparation for cloning the line.

Peptide-specific cell lines were cloned by limiting dilution analysis with irradiated (20,000 rads) L762P peptide-pulsed EL4 A2Kb tumor cells ( $1 \times 10^4$  cells/well) as stimulators and irradiated (3000 rads) A2/K<sup>b</sup>-transgenic spleen cells as feeders ( $5 \times 10^5$  cells/ well) grown in the presence of 10U/ml IL-2. On day 7, cells were restimulated as before. On day 14, clones that were growing were isolated and maintained in culture.

Cell lines specific for L762P-87 (SEQ ID NO: 226; corresponding to amino acids 87-95 of SEQ ID NO: 161), L726P-145 (SEQ ID NO: 227; corresponding to amino acids 145-153 of SEQ ID NO: 161), L726P-585 (SEQ ID NO: 228; corresponding to amino acids 585-593 of SEQ ID NO: 161), L762P-425 (SEQ ID NO: 229; corresponding to amino acids 425-433 of SEQ ID NO: 161), L762P(10)-424 (SEQ ID NO: 230; corresponding to amino acids 424-433 of SEQ ID NO: 161) and L762P(10)-458 (SEQ ID NO: 231; corresponding to amino acids 458-467 of SEQ ID

NO: 161) demonstrated significantly higher reactivity (as measured by percent specific lysis) against L762P peptide-pulsed EL4-A2/K<sup>b</sup> tumor target cells than control peptide-pulsed EL4-A2/K<sup>b</sup> tumor target cells.

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## EXAMPLE 7

IDENTIFICATION OF CD4 IMMUNOGENIC T CELL EPITOPES DERIVED  
FROM THE LUNG CANCER ANTIGEN L762P

CD4 T cell lines specific for the antigen L762P (SEQ ID NO: 161) were  
10 generated as follows.

A series of 28 overlapping peptides were synthesized that spanned approximately 50% of the L762P sequence. For priming, peptides were combined into pools of 4-5 peptides, pulsed at 20 micrograms/ml into dendritic cells for 24 hours. The dendritic cells were then washed and mixed with positively selected CD4<sup>+</sup> T cells in 96  
15 well U-bottomed plates. Forty cultures were generated for each peptide pool. Cultures were restimulated weekly with fresh dendritic cells loaded with peptide pools. Following a total of 3 stimulation cycles, cells were rested for an additional week and tested for specificity to antigen presenting cells (APC) pulsed with peptide pools using interferon-gamma ELISA and proliferation assays. For these assays, adherent  
20 monocytes loaded with either the relevant peptide pool or an irrelevant peptide were used as APC. T cell lines that appeared to specifically recognize L762P peptide pools both by cytokine release and proliferation were identified for each pool. Emphasis was placed on identifying T cells with proliferative responses. T cell lines that demonstrated either both L762P-specific cytokine secretion and proliferation, or strong proliferation  
25 alone were further expanded to be tested for recognition of individual peptides from the pools, as well as for recognition of recombinant L762P. The source of recombinant L762P was *E. coli*, and the material was partially purified and endotoxin positive. These studies employed 10 micrograms of individual peptides, 10 or 2 micrograms of an irrelevant peptide, and 2 or 0.5 micrograms of either L762P protein or an irrelevant,  
30 equally impure, *E. coli* generated recombinant protein. Significant interferon-gamma production and CD4 T cell proliferation was induced by a number of L762P-derived



peptides in each pool. The amino acid sequences for these peptides are provided in SEQ ID NO: 232-251. These peptides correspond to amino acids 661-680, 676-696, 526-545, 874-893, 811-830, 871-891, 856-875, 826-845, 795-815, 736-755, 706-725, 706-725, 691-710, 601-620, 571-590, 556-575, 616-635, 646-665, 631-650, 541-560  
5 and 586-605, respectively, of SEQ ID NO: 161.

CD4 T cell lines that demonstrated specificity for individual L762P-derived peptides were further expanded by stimulation with the relevant peptide at 10 micrograms/ml. Two weeks post-stimulation, T cell lines were tested using both proliferation and IFN-gamma ELISA assays for recognition of the specific peptide. A  
10 number of previously identified T cells continued to demonstrate L762P-peptide specific activity. Each of these lines was further expanded on the relevant peptide and, following two weeks of expansion, tested for specific recognition of the L762P-peptide in titration experiments, as well as for recognition of recombinant *E. coli*-derived L762P protein. For these experiments, autologous adherent monocytes were pulsed with either  
15 the relevant L762P-derived peptide, an irrelevant mammaglobin-derived peptide, recombinant *E. coli*-derived L762P (approx. 50% pure), or an irrelevant *E. coli*-derived protein. The majority of T cell lines were found to show low affinity for the relevant peptide, since specific proliferation and IFN-gamma ratios dramatically decreased as L762P peptide was diluted. However, four lines were identified that demonstrated  
20 significant activity even at 0.1 micrograms/ml peptide. Each of these lines (referred to as A/D5, D/F5, E/A7 and E/B6) also appeared to specifically proliferate in response to the *E. coli*-derived L762P protein preparation, but not in response to the irrelevant protein preparation. The amino acid sequences of the L762P-derived peptides recognized by these lines are provided in SEQ ID NO: 234, 249, 236 and 245,  
25 respectively. No protein specific IFN-gamma was detected for any of the lines. Lines A/D5, E/A7 and E/B6 were cloned on autologous adherent monocytes pulsed with the relevant peptide at 0.1 (A/D5 and E/A7) or 1 (D/F5) microgram/ml. Following growth, clones were tested for specificity for the relevant peptide. Numerous clones specific for the relevant peptide were identified for lines A/D5 and E/A7.

## EXAMPLE 8

## PROTEIN EXPRESSION OF LUNG TUMOR-SPECIFIC ANTIGENS

5 a) Expression of L514S in *E. coli*

The lung tumor antigen L514S (SEQ ID NO: 89) was subcloned into the expression vector pE32b at NcoI and NotI sites, and transformed into *E. coli* using standard techniques. The protein was expressed from residues 3-153 of SEQ ID NO: 89. The expressed amino acid sequence and the corresponding DNA sequence are  
10 provided in SEQ ID NO: 252 and 253, respectively.

b) Expression of L762P

Amino acids 32-944 of the lung tumor antigen L762P (SEQ ID NO: 161), with a 6X His Tag, were subcloned into a modified pET28 expression vector,  
15 using kanamycin resistance, and transformed into BL21 CodonPlus using standard techniques. Low to moderate levels of expression were observed. The determined DNA sequence of the L762P expression construct is provided in SEQ ID NO: 254.

From the foregoing it will be appreciated that, although specific  
20 embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

## CLAIMS

1. An isolated polypeptide, comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (a) sequences recited in SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349;
- (b) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349 under moderately stringent conditions; and
- (c) complements of sequences of (a) or (b).
2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158,

160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349 or a complement of any of the foregoing polynucleotide sequences.

5

3. An isolated polypeptide comprising a sequence recited in any one of SEQ ID NO: 110, 112, 114, 152, 155, 156, 159, 161, 165, 166, 169, 170, 172, 174, 176, 226-252, 346, 348 and 350.

4. An isolated polynucleotide encoding at least 15 amino acid  
10 residues of a lung tumor protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29,  
15 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349 or a  
20 complement of any of the foregoing sequences.

5. An isolated polynucleotide encoding a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO:  
25 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317,  
30 323, 345, 347 and 349 or a complement of any of the foregoing sequences.

6. An isolated polynucleotide, comprising a sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349.

7. An isolated polynucleotide, comprising a sequence that hybridizes to a sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349 under moderately stringent conditions.

8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.

9. An expression vector, comprising a polynucleotide according to any one of claims claim 4-8.

10. A host cell transformed or transfected with an expression vector according to claim 9.

11. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a lung tumor protein that comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84,

86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and  
5 349\_ or a complement of any of the foregoing polynucleotide sequences.

12. A fusion protein, comprising at least one polypeptide according to claim 1.

10 13. A fusion protein according to claim 12, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.

14. A fusion protein according to claim 12, wherein the fusion  
15 protein comprises a T helper epitope that is not present within the polypeptide of claim 1.

15. A fusion protein according to claim 12, wherein the fusion protein comprises an affinity tag.

20

16. An isolated polynucleotide encoding a fusion protein according to claim 12.

17. A pharmaceutical composition, comprising a physiologically  
25 acceptable carrier and at least one component selected from the group consisting of:

- (a) a polypeptide according to claim 1;
- (b) a polynucleotide according to claim 4;
- (c) an antibody according to claim 11;
- (d) a fusion protein according to claim 12; and
- 30 (e) a polynucleotide according to claim 16.

18. A vaccine comprising an immunostimulant and at least one component selected from the group consisting of:

- (a) a polypeptide according to claim 1;
- 5 (b) a polynucleotide according to claim 4;
- (c) an antibody according to claim 11;
- (d) a fusion protein according to claim 12; and
- (e) a polynucleotide according to claim 16.

10 19. A vaccine according to claim 18, wherein the immunostimulant is an adjuvant.

20. A vaccine according to any claim 18, wherein the immunostimulant induces a predominantly Type I response.

15

21. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 17.

20 22. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 18.

23. A pharmaceutical composition comprising an antigen-presenting  
25 cell that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.

24. A pharmaceutical composition according to claim 23, wherein the antigen presenting cell is a dendritic cell or a macrophage.

30

25. A vaccine comprising an antigen-presenting cell that expresses a polypeptide comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

5 (a) sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171,  
10 173, 175, 177-224, 255-337, 345, 347 and 349 under moderately stringent conditions; and

(c) complements of sequences of (i) or (ii);  
in combination with an immunostimulant.

15 26. A vaccine according to claim 25, wherein the immunostimulant is an adjuvant.

27. A vaccine according to claim 25, wherein the immunostimulant induces a predominantly Type I response.

20

28. A vaccine according to claim 25, wherein the antigen-presenting cell is a dendritic cell.

29. A method for inhibiting the development of a cancer in a patient,  
25 comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

30 (a) sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and



349;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 under moderately stringent conditions; and

(c) complements of sequences of (i) or (ii) encoded by a polynucleotide recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349; and thereby inhibiting the development of a cancer in the patient.

30. A method according to claim 29, wherein the antigen-presenting cell is a dendritic cell.

31. A method according to any one of claims 21, 22 and 29, wherein the cancer is lung cancer.

32. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) polynucleotides recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349; and

(ii) complements of the foregoing polynucleotides; wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the antigen from the sample.

33. A method according to claim 32, wherein the biological sample is blood or a fraction thereof.

34. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 32.

5

35. A method for stimulating and/or expanding T cells specific for a lung tumor protein, comprising contacting T cells with at least one component selected from the group consisting of:

(a) polypeptides comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349;

15

(ii) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 under moderately stringent conditions; and

20

(iii) complements of sequences of (i) or (ii);

(b) polynucleotides encoding a polypeptide of (a); and

(c) antigen presenting cells that express a polypeptide of (a);

under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

25

36. An isolated T cell population, comprising T cells prepared according to the method of claim 35.

37. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 36.

30

38. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

5 (a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient with at least one component selected from the group consisting of:

(i) polypeptides comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

10 (1) sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349;

(2) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 15  
160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 under moderately stringent conditions; and

(3) complements of sequences of (1) or (2);

(ii) polynucleotides encoding a polypeptide of (i); and

(iii) antigen presenting cells that expresses a polypeptide of  
20 (i);

such that T cells proliferate; and

(b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

25 39. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient with at least one component selected from the group consisting of:

(i) polypeptides comprising at least an immunogenic portion  
30 of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence

selected from the group consisting of:

- (1) sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349;
- 5 (2) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 under moderately stringent conditions; and
- (3) complements of sequences of (1) or (2);
- 10 (ii) polynucleotides encoding a polypeptide of (i); and
- (iii) antigen presenting cells that express a polypeptide of (i);  
such that T cells proliferate;
- (b) cloning at least one proliferated cell to provide cloned T cells;
- and
- 15 (c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.

40. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

- 20 (a) contacting a biological sample obtained from a patient with a binding agent that binds to a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 or a complement of any of the
- 25 foregoing polynucleotide sequences;
- (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and
- (c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

41. A method according to claim 40, wherein the binding agent is an

antibody.

42. A method according to claim 43, wherein the antibody is a monoclonal antibody.

5

43. A method according to claim 40, wherein the cancer is lung cancer.

44. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent;

(c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

(d) comparing the amount of polypeptide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

45. A method according to claim 44, wherein the binding agent is an antibody.

46. A method according to claim 45, wherein the antibody is a monoclonal antibody.

30

47. A method according to claim 44, wherein the cancer is a lung

cancer.

48. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

- 5 (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347  
10 and 349 or a complement of any of the foregoing polynucleotide sequences;
- (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and
- (c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the  
15 presence or absence of a cancer in the patient.

49. A method according to claim 48, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

20

50. A method according to claim 48, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

25 51. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

- (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a  
30 polynucleotide sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347

and 349 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;

(c) repeating steps (a) and (b) using a biological sample obtained  
5 from the patient at a subsequent point in time; and

(d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

10 52. A method according to claim 51, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

15 53. A method according to claim 51, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

54. A diagnostic kit, comprising:

(a) one or more antibodies according to claim 11; and  
20 (b) a detection reagent comprising a reporter group.

55. A kit according to claim 54, wherein the antibodies are immobilized on a solid support.

25 56. A kit according to claim 54, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.

57. A kit according to claim 54, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent  
30 groups, enzymes, biotin and dye particles.

58. An oligonucleotide comprising 10 to 40 contiguous nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349 or a complement of any of the foregoing polynucleotides.

59. A oligonucleotide according to claim 58, wherein the oligonucleotide comprises 10-40 contiguous nucleotides recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349.

20

60. A diagnostic kit, comprising:

- (a) an oligonucleotide according to claim 59; and
- (b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.

25



## SEQUENCE LISTING

<110> Corixa Corporation et al.

<120> COMPOUNDS AND METHODS FOR THERAPY  
AND DIAGNOSIS OF LUNG CANCER

<130> 210121.45501PC

<140> PCT

<141> 2000-04-03

<160> 350

<170> FastSEQ for Windows Version 3.0

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<211> 315

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<213> Homo sapien

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ttcatctcca gcagagacaa cggaggaggc tcccaccagg acggttctca ttatttatat	180
gttaatatgt ttgtaaaactc atgtacagtt ttttttgggg ggggaagcaat gggaanggta	240
naaattacaa atagaatcat ttgctgtaat ccttaaattgg caaacgggtca ggccacgtga	300
aaaaaaaaaa aaaaaa	315

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<211> 380

<212> DNA

<213> Homo sapien

<400> 2

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atatatataa acaaatacaa aaagttttga gtggttcagc ttttttattt tttttaatgg	120
cataactttt aacaacactg ctctgtaatg ggttgaactg tggtaactcag actgagataa	180
ctgaaatgag tggatgtata gtgttattgc ataattatcc cactatgaag caaagggact	240
ggataaattc ccagtctaga ttattagcct ttgttaacca tcaagcacct agaagaagaa	300
ttattgaaa ttttgtcctc tgtaactggc actttgggggt gtgacttata ttttgccttt	360
gtaaaaaaaa aaaaaaaaaa	380

<210> 3

<211> 346

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

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 <222> (1)...(346)  
 <223> n = A,T,C or G

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 catcctcacc atacaccatc cacttttccaa taacatttta taacttttctaa aattgtaagt 120  
 atacaattgt acttttctttg gatttttcata acaaataac catagactgt taatttttatt 180  
 gaagtttcct taatggaatg agtcattttt gtcttgtgct tttgagggtta cctttgcttt 240  
 gacttccaac aatttgatca tatagtgttg agctgtggaa atctttaagt ttattctata 300  
 gcaataattt ctattnnnag annccngggn naaaannann annaaa 346

<210> 4  
 <211> 372  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(372)  
 <223> n = A,T,C or G

<400> 4  
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 tctcttctcc aagttgtgct ttgtggggac aatcattctt tgaacattag agaggaaggc 180  
 agttcaagct gttgaaaaga ctattgctta tttttgtttt taaagacctt cttgacgtca 240  
 tgtggacagt gcacgtgcct tacgctacat cttgttttct aggaagaagg ggatgcnggg 300  
 aaggantggg tgctttgtga tggataaaac gntctaaataa cacaccttta ctttttgaaa 360  
 aaaacaaaac aa 372

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 <212> DNA  
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 gcataaagcc aatgtagtcc agtttctaag atcatgttcc aagctaactg aatcccactt 180  
 caatacacac tcatgaactc ctgatggaac aataacaggc ccaagcctgt ggtatgatgt 240  
 gcacacttgc tagactcaga aaaaatacta ctctcataaa tgggtgggag tttttgggt 300  
 gacaacctac tttgcttggc tgagtgaagg aatgatattc atatnttcat ttattccatg 360  
 gacatttagt tagtgctttt tatataccag gcattgatgt gagtgacact cttgtgtata 420  
 tntccaaatn ttngtncngt cgctgcacat atctgaaatc ctatattaag antttcccaa 480  
 natgangtcc ctgggttttc cagccactt gatcngtcaa ngatctcacc tctgntgtc 540  
 ctaaaacnt ctncnnang gttagaacngg acctctcttc tcccttcccg aanaatnaag 600  
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698

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 <211> 740  
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 <213> Homo sapien  
  
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 <223> n = A,T,C or G

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 gccaatattt ccttataatc atccataaca tttatactac atttgtaaga gaatatgcac 180  
 gtgaaactta acactttata aggtaaaaat gaggtttcca agatttaata atctgatcaa 240  
 gttcttggtta tttccaaata gaatggactt ggtctgttaa ggggctaagg gagaagaaga 300  
 agataagggt aaaagtgtgt aatgaccaa cattctaaaa gaaatgcaa aaaaaattta 360  
 ttttcaagcc ttcgaactat ttaaggaaag caaaatcatt tcctanatgc atatcatttg 420  
 tgagantttc tcantaatat cctgaatcat tcatttcagc tnaggcttca tgttgactcg 480  
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 tttcctttaa ntgtgaanta ttnacangaa attttctctt tnanagttct tnatagggtt 600  
 aggggtgtgg gaaaagcttc taacaatctg tagtgttncg tgttatctgt ncagaaccan 660  
 aatnacggat cgnangaagg actgggtcta tttacangaa cgaatnatct ngtnnnntgt 720  
 gtnnncaact ccngggagcc 740

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 <211> 670  
 <212> DNA  
 <213> Homo sapien  
  
 <220>  
 <221> misc\_feature  
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 <223> n = A,T,C or G

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 cttgggatgc aggagctggt cgggggccac agcaagaccg cgagttcctg gcgcacagcg 180  
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 cgtctggaga taaaaccatt cgcactctgg atgtgaggac tacaaaatgc attgccactg 420  
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 tagcnacaag gatgatgtgg tgactttatt gatgccaaag aaccccgctc caaagcaaaa 540  
 aaacanttcc aanttcgaag tcaccnaaat ctccctggaac aatgaacatn aatatnttct 600  
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 natccacccc 670

<210> 8  
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 <212> DNA  
 <213> Homo sapien

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 <221> misc\_feature  
 <222> (1) ... (689)  
 <223> n = A,T,C or G

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 cacctagcat tgcctactta gccccctgaa ttaacagagc ccaattgaga caaaccctg 180  
 gcaacaggaa attcaagga gaaaaagtaa gcaacttggg ctaggatgag ctgactccct 240  
 tagagcaaag ganagacagc cccattacc aaataccatt tttgcctggg gcttgtgcag 300  
 ctggcagtg tctgccccca gcatggcacc ttatngtttt gatagcaact tcgttgaatt 360  
 ttcaccaact tattacttga aattataata tagcctgtcc gtttgcctgt tccaggctgt 420  
 gatatatntt cctagtgggt tgacttttaa aataaatnag gtttantttt cccccccnn 480  
 cnntnctncc nntcnctenn cnntcccccc cnotengtcc tccnnnnntn gggggggccn 540  
 cccccnccgn ggacccccct ttgggtccctt agtggaggtt natggcccct ggnnttatcc 600  
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 aagcctaagt ttntaccctg ggggtcccc 689

<210> 9  
 <211> 674  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (674)  
 <223> n = A,T,C or G

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 gaaaaaagcg aggttttttt gccaccttgg taaaggccag ttcactgcta tagaactgct 180  
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 caaaaacatt agctgttctg tctttcaatt tcaagttatt ttggagactg cctccatgtg 480  
 agttaattac tttgctctgg aactagcatt attgtcatta tcatcacatt ctgtcatcat 540  
 catctgaata atattgtgga tttccccctc tgcttgcac ttcttttgac tctctggga 600  
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 <212> DNA  
 <213> Homo sapien

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 <223> n = A,T,C or G

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ccttaagtgt	ttctgtcatt	gttcaagtgt	atcttctgta	acagaaacat	atttggaatg	180
tttttctttt	ccccttataa	attgtaattc	ctgaaatact	gctgctttta	aaagtccac	240
tgtcagatta	tattatctaa	caattgaata	ttgtaaatat	acttgtctta	cctctcaata	300
aaagggtact	tttctattan	nnagnngnnn	gnnnnataaa	anaaaa		346

&lt;210&gt; 11

&lt;211&gt; 602

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 11

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gatgttaagc	tttttgaaaa	gtttagggtta	aacctactgt	tgtagatta	atgtatttgt	120
tgcttccctt	tatctggaat	gtggcattag	cttttttatt	ttaaccctct	ttaattctta	180
ttcaattcca	tgacttaagg	ttggagagct	aaacactggg	atcttttgat	aacagactga	240
cagttttgca	taattataat	cggcattgta	catagaaagg	atatggctac	cttttggtta	300
atctgcactt	tctaaatatc	aaaaaaggga	aatgaagtta	taaatcaatt	tttgataaat	360
ctgtttgaaa	catgagtttt	atttgcttaa	tattagggct	ttgccccttt	tctgtaagtc	420
tcttgggata	ctgtgtagaa	ctgttctcat	taaacaccaa	acagttaagt	ccattctctg	480
gtactagcta	caaattcggg	ttcatattct	acttaacaat	ttaaataaac	tgaaatatatt	540
ctagatgggc	tacttctgtt	catataaaaa	caaaacttga	tttccaaaaa	aaaaaaaaaa	600
aa						602

&lt;210&gt; 12

&lt;211&gt; 685

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (685)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 12

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gcattgcattt	gtaacatgat	tagtagattt	gaatatatag	atgtagtatn	ttgggtatct	180
agggtgtttta	tcattatgta	aaggaattaa	agtaaaggac	tttgtagtgt	tttttattaa	240
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angtagtgcc	ctcgtagggt	tcacgtggan	tantggganc	aggccgnncn	gtnanaagaa	480
ancanngtga	nagtttctnc	gtngangcng	aactgtccct	gngccnnnac	gctcccanaa	540
cntntccaat	ngacaatcga	gtttccnnnc	tcngnaaacc	tngccgnnnn	cnngcccnnc	600
cantntgnta	accccgcgcc	cggatcgctc	tcnnntcggt	ctcncncnaa	ngggntttcn	660
cnnccgcggt	cncnnccccg	cnncc				685

&lt;210&gt; 13

&lt;211&gt; 694

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

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tttctctgtg	tgtgcaaatg	tgtgtttgtg	atccattttt	tttttttttt	taggacacct	240
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tcaccctctt	ttccccccat	gctttttgcc	ctagttttata	acaaaggaat	gatgatgatt	360
taaaaagtag	ttctgtatct	tcagtatctt	ggtcttccag	aaccctctgg	ttgggaaggg	420
gatcattttt	tactgggtcat	ttccctttgg	agtgtactac	tttaacagat	ggaaagaact	480
cattggccat	ggaaacagcc	gangtggttg	gagccagcag	tgcatggcac	cgtccggcat	540
ctggcntgat	tggtctggct	gccgtcattg	tcagcacagt	gccatgggac	atggggaana	600
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ccaagtgcac	caaataacctg	cngtnccgat	ntaaattcat	cttctggctt	gccgggattg	180
ctgtccntgc	cattggacta	nggctccgat	ncgactctca	gaccanganc	atcttcganc	240
naganactaa	tnatnatnt	tccagcttct	acacaggagt	ctatattctg	atcggatccg	300
gncccctcnt	gatgctgggtg	ggcttccctga	gctgctgcgg	ggctgtgcaa	gagtcccant	360
gcatgctggg	actgttcttc	ggcttctctt	tggtgatatn	cgccattgaa	atacctgcgg	420
ccatctgggg	atattccact	ncgatnatgt	gattaaggaa	ntccacggag	ttttacaagg	480
acacgtacaa	cnacctgaaa	accnnggatg	anccccaccg	ggaancnctg	aangccatcc	540
actatgcgtt	gaactgcaat	ggtttggtctg	gggnccttga	acaatttaat	cncatacatc	600
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 <222> (1)...(695)  
 <223> n = A,T,C or G

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ttaaaaaagg	gcctgaaaaa	aggggagcca	caaattctgtc	tgcttcctca	cnttantcnt	180
tggcaaatna	gcattctgtc	tcnttggtg	cngcctcanc	ncaaaaaanc	ngaactcnat	240
cngggccagg	aatacatctc	ncaatnaacn	aaattganca	aggcnntggg	aaatgccnga	300
tgggattatc	ntccgcttgt	tganccttcta	agtttctnttc	ccttcattcn	accctgccag	360
ccnagttctg	ttagaaaaat	gccngaattc	naacnccggt	tttctactc	ngaatttaga	420
tctncanaaa	cttccctggcc	acnattcnaa	ttnanggnca	cgnacanatn	ccttccatna	480
ancncacccc	acntttgana	gccangacaa	tgactgcntn	aantgaaggc	ntgaaggaan	540
aactttgaaa	ggaaaaaaa	ctttgtttcc	ggccccttcc	aacncttctg	tgttnancac	600
tgccttctng	naaccctgga	agcccnnga	cagtgttaca	tgttgttcta	nnaaacngac	660
ncttnaatnt	cnatcttccc	nanaacgatt	ncncc			695

&lt;210&gt; 16

&lt;211&gt; 669

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (669)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 16

cgccgaagca	gcagcgcagg	ttgtccccgt	tccccctccc	ccttcccttc	tccggttgcc	60
tccccgggcc	ccttacactc	cacagtcccg	gtccccccat	gtcccagaaa	caagaagaag	120
agaaccctgc	ggaggagacc	ggcgaggaga	agcaggacac	gcaggagaaa	gaaggatttc	180
tgectgagag	agctgaagag	gcaaagctaa	aggccaaata	cccaagccta	ggacaaaagc	240
ctggaggctc	cgacttcttc	atgaagagac	tccagaaaagg	gcaaaaagtac	tttgactcng	300
gagactacaa	catggccaaa	gccaacatga	agaataagca	gctgccaaagt	gcangaccag	360
acaagaacct	ggtgactggt	gatcacatcc	ccaccccaca	ggatctgccc	agagaaagtc	420
ctcgtctctc	accagcaagc	ttgcgggttg	ccaagttgaa	tgatgctgcc	ggggctctgc	480
canatctgag	acgttctccc	ccttccccca	cccgggtcct	gtgctggctc	ctgcccttcc	540
tgcttttgca	gccangggtc	aggaagtggc	ncnggtngtg	gctggaaagc	aaaacctttt	600
cctgttggtg	tcccacccat	ggagcccctg	gggcgagccc	angaacttga	ncctttttgt	660
tntcttncc						669

&lt;210&gt; 17

&lt;211&gt; 697

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (697)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 17

gcaagatatg	gacaactaag	tgagaaggta	atnctctact	gctctagntn	ctcengggenn	60
gacgcgtga	ggagannnac	gctggcccan	ctgcgggcca	cacacgggga	tcttggtnat	120
gcctgcccان	gggancccca	nencteggan	cccatntcac	accegngccn	tncgcccان	180
ncctggcten	cnengcccng	nccagctcnc	gncccccctc	gcnnnctcn	ttnnctctc	240
cnccccctcc	nnaacnacct	cctaccnccg	gtccccctcc	cagccccccc	ccgcaancct	300
ccacnacncc	ntcnncncca	anencnctc	genctcngcc	cngccccctc	gccccccgcc	360
cnacnncng	cgntcccccg	cgncgcngc	ctnccccctc	cccacnacag	ncncaccgcg	420
agncaagcnc	tccgcccنct	gacgcccنn	cccgccgcgc	tcaccttcac	ggncnncng	480
ccccgcctnc	ncnctgcnc	gccgnccngg	cgccccgcgc	cnnccngntn	ccnccngngg	540

```

ccccngcngn angcngtgcg cnnangncc gngccggnncn ncaccctccg nccnccgccc      600
cgcccgtctg gggtcccgcc cncgcgntc antcccncc cntncgccc ctntccgntc      660
cnnnctcnc gctcngcgcn cgcncncnc ccccccc      697

```

```

<210> 18
<211> 670
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (670)
<223> n = A,T,C or G

```

```

<400> 18
ctcgtgtgaa ggggtgcagta cctaagccgg agcggggtag aggcggggccg gcaccccctt      60
ctgacctcca gtgccgccgg cctcaagatc agacatggcc cagaacttga acgacttggc      120
gggacggctg cccgccgggc cccggggcat gggcacggcc ctgaagctgt tgctgggggc      180
cggcgccgtg gcctacggtg tgccggaatc tgtgttcacc gtggaaggcg ggcnagagc      240
catcttcttc aatcggatcg gtggagtgc caggacacta tcctggggccg anggccttca      300
cttcaggatc cttggttcca gtacccanc atctatgaca ttcggggccag acctcgaaaa      360
aatctcctcc ctacaggctc caaagacctc cagatggtga atatctccct gcgagtgttg      420
tctcgaccaa tgctcangaa cttcctaaca tgttccancg cctaagggtc ggactacnaa      480
gaacgantgt tgccgtccat tgtcacgaag tgctcaagaa tttnggtggc caagttcaat      540
gncctcacnn ctgatcnccc agcggggcca agttanccct gggtgatccc cgggganctg      600
acnnaaaagg gccaaaggact tcccctcacc ctggataatg tggccntcac aaagctcaac      660
tttanccacc      670

```

```

<210> 19
<211> 606
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (606)
<223> n = A,T,C or G

```

```

<400> 19
actagtgcc accctcagtc ccaggccagt tctctgaatg tcgaggagtt ccaggatctc      60
tggcctcagt tgtccttggt tattgatggg ggacaaattg gggatggcca gagccccgag      120
tgtcgcttg gctcaactgt ggttgatttg tctgtgccc gaaagtgttg catcatctgt      180
ccaggctgtg ccttggaag tactacagcc atcctccaac agaagtacgg actgctcccc      240
tcacatgcgt cctacctgtg aaactctggg aagcaggaag gcccaagacc tgggtgctgga      300
tactatgtgt ctgtccactg acgactgtca aggcctcatt tgccaggcc accggagcta      360
gggcactagc ctgactttta aggcagtgtg tctttctgag cactgtagac caagcccttg      420
gagctgctgg tttagccttg cacctgggga aaggatgtat ttatttgtat tttcatatat      480
cagccaaaag ctgaatggaa aagttnagaa cattcctagg tggccttatt ctaataagtt      540
tcttctgtct gttttgtttt tcaattgaaa agttattaaa taacagattt agaactagtt      600
gagacc      606

```

```

<210> 20
<211> 449
<212> DNA
<213> Homo sapien

```



<400> 20  
 actagtaaac aacagcagca gaaacatcag tatcagcagc gtcgccagca ggagaatatg 60  
 cagcgccaga gccgaggaga acccccgcgc cctgaggagg acctgtccaa actcttcaaa 120  
 ccaccacagc cgctgccag gatggactcg ctgctcattg caggccagat aaacacttac 180  
 tgccagaaca tcaaggagtt cactgcccac aacttaggca agctcttcat ggcccaggct 240  
 cttcaagaat acaacaacta agaaaaggaa gtttcagaa aagaagttaa catgaactct 300  
 tgaagtcaca ccagggcaac tcttggaaga aatataattg catattgaaa agcacagagg 360  
 atttcttttag tgtcattgcc gattttggct ataacagtgt ctttctagcc ataataaaat 420  
 aaaacaaaat cttgactgct tgctcaaaa 449

<210> 21

<211> 409

<212> DNA

<213> Homo sapien

<400> 21  
 tatcaatcaa ctggtgaata attaaacaat gtgtggtgtg atcatacaaa gggtaccact 60  
 caatgataaa aggaacaagc tgcctatatg tggaacaaca tggatgcatt tcagaaactt 120  
 tatgttgagt gaaagaacaa acacggagaa catactatgt gggtctcttt atgtaacatt 180  
 acagaaataa aaacagaggc aaccaccttt gaggcagtat ggagtgagat agactggaaa 240  
 aaggaaggaa ggaaactcta cgctgatgga aatgtctgtg tcttcattgg gtggtagtta 300  
 tgtggggata tacatttgct aaaatttatt gaactatata cttaaagaact ctgcatttta 360  
 ttgggatgta aataatacct caattaaaaa gacaaaaaaa aaaaaaaaaa 409

<210> 22

<211> 649

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (649)

<223> n = A,T,C or G

<400> 22  
 acaatttttca ttatcttaag cacattgtac atttctacag aacctgtgat tattctcgca 60  
 tgataaggat ggtacttgca tatggtgaat tactactggt gacagtttcc gcagaaatcc 120  
 tatttcagtg gaccaacatt gtggcatggc agcaaattgcc aacattttgt ggaatagcag 180  
 caaatctaca agagaccctg gttgggtttt cgttttgttt tctttgtttt ttcccccttc 240  
 tcctgaatca gcagggatgg aangagggtg gggaagttaa gaattactcc ttccagtagt 300  
 agctctgaag tgtcacattt aatatcagtt ttttttaaac atgattctag ttnaatgtag 360  
 aagagagaag aaagaggaag tgttcacttt ttttaatacac tgatttagaa atttgatgtc 420  
 ttatatcagt agttctgagg tattgatagc ttgctttatt tctgccttta cgttgacagt 480  
 gttgaagcag ggtgaataac taggggcata tatatttttt ttttttgtaa gctgtttcat 540  
 gatgttttct ttggaatttc cggataagtt caggaaaaca tctgcatggt gttatctagt 600  
 ctgaagtton tatccatctc attacaacaa aaacncccag aacggnntg 649

<210> 23

<211> 669

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

&lt;222&gt; (1)...(669)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 23

actagtgcg	tactggctga	aatccctgca	ggaccaggaa	gagaaccagt	tcagactttg	60
tactctcagt	caccagctct	ggaattagat	aaattccttg	aagatgtcag	gaatgggac	120
tatcctctga	cagccttttg	gctgcctcgg	ccccagcagc	cacagcagga	ggaggtgaca	180
tcacctgtcg	tgccccctc	tgtcaagact	ccgacacctg	aaccagctga	ggaggagact	240
cgcaaggtgg	tgctgatgca	gtgcaacatt	gagtcgggtg	aggagggagt	caaacaccac	300
ctgacacttc	tgctgaagt	ggaggacaaa	ctgaaccggc	acctgagctg	tgacctgatg	360
ccaaatgaga	atatccccga	gttggcggct	gagctgggtg	agctgggctt	cattagttag	420
gctgaccaga	gccggttgac	ttctctgcta	gaagagactt	gaacaagttc	aattttgcca	480
ggaacagtac	cctcaactca	gccgctgtca	ccgtctcctc	ttagagctca	ctcggggcag	540
gcccgtgatc	gcgctgtggc	tgtcctggac	gtgctgcacc	ctctgtcctt	ccccccagtc	600
agtattacct	gtgaagccct	tcctcctttt	attattcagg	anggctgggg	gggctccttg	660
nttctaacc						669

&lt;210&gt; 24

&lt;211&gt; 442

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 24

actagtacca	tcttgacaga	ggatacatgc	tcccaaaacg	tttgttacca	cacttaaaaa	60
tcactgccat	cattaagcat	cagtttcaaa	attatagcca	ttcatgattt	actttttcca	120
gatgactatc	attattctag	tcctttgaat	ttgtaagggg	aaaaaaaaca	aaaacaaaaa	180
cttacgatgc	actttttctc	agcacatcag	atttcaaatt	gaaaattaaa	gacatgctat	240
ggtaatgcac	ttgctagtac	tacacacttt	ggtacaacaa	aaaacagagg	caagaaacaa	300
cggaaagaga	aaagccttcc	tttgttggcc	cttaaactga	gtcaagatct	gaaatgtaga	360
gatgatctct	gacgatacct	gtatgttctt	attgtgtaaa	taaaattgct	ggtatgaaat	420
gacctaaaaa	aaaaaaaaga	aa				442

&lt;210&gt; 25

&lt;211&gt; 656

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(656)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 25

tgcaagtacc	acacactgtt	tgaattttgc	acaaaaagtg	actgtaggat	caggtgatag	60
ccccggaatg	tacagtgtct	tggtgcacca	agatgccttc	taaaggctga	cataccttgg	120
accctaattg	ggcagagagt	atagccctag	cccagtgggtg	acatgaccac	tccttttggg	180
aggcctgagg	tagaggggag	tggtatgtgt	tttctcagtg	gaagcagcac	atgagtgggt	240
gacaggatgt	tagataaagg	ctctagttag	gggtgtcattg	tcatttgaga	gactgacaca	300
ctcctagcag	ctggtaaagg	gggtgtggan	gccatggagg	anctctagaa	acatttagcat	360
gggctgatct	gattacttcc	tggtatcccg	ctcactttta	tggaagtctt	tattagangg	420
atgggacagt	tttccatata	cttgctgtgg	agctctggaa	cactctctaa	atttccctct	480
attaaaaatc	actgccctaa	ctacacttcc	tccttgaagg	aatagaaatg	gaactttctc	540
tgacatannt	cttggtcatg	ggagccagcc	acaaatgana	atctgaacgt	gtccaggttt	600
ctcctganac	tcactctacat	agaatttggtt	aaaccctccc	ttggaataag	gaaaaa	656

<210> 26  
 <211> 434  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (434)  
 <223> n = A,T,C or G

<400> 26  
 actagttcag actgccacgc caaccccaga aaatacccca catgccagaa aagtgaagtc 60  
 ctaggtgttt ccatctatgt ttcaatctgt ccatctacca ggcctcgca taaaaacaaa 120  
 acaaaaaaac gctgccaggt tttagaagca gttctggtct caaaaccatc aggatcctgc 180  
 caccagggtt cttttgaaat agtaccacat gtaaaagga atttggcttt cacttcatct 240  
 aataactgaa ttgtcaggct ttgattgata attgtagaaa taagtagcct tctgttgagg 300  
 gaataagtta taatcagtat tcactctctt gttttttgtc actcttttct ctctaattgt 360  
 gtcatttgta ctgtttgaaa aatatttctt ctatnaaatt aaactaacct gccttaaaaa 420  
 aaaaaaaaaa aaaa 434

<210> 27  
 <211> 654  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (654)  
 <223> n = A,T,C or G

<400> 27  
 actagtccaa cacagtcaga aacattgttt tgaatcctct gtâaaccaag gcattaatct 60  
 taataaacca ggatccattt aggtaccact tgatataaaa aggatatcca taatgaatat 120  
 ttataactgc atcctttaca ttagccacta aatacgttat tgcttgatga agacctttca 180  
 cagaatccta tggattgcag catttcactt ggctacttca taccatgcc ttaaagaggg 240  
 gcagtttctc aaaagcagaa acatgccgcc agttctcaag ttttcctcct aactccattt 300  
 gaatgtaagg gcagctggcc cccaatgtgg ggagggtccga acattttctg aattcccatt 360  
 ttcttgttcg cggctaaatg acagtttctg tcattactta gattccgac tttcccaaag 420  
 gtgttgattt acaaagaggc cagctaatag cagaaatcat gaccctgaaa gagagatgaa 480  
 attcaagctg tgagccaggc agganctcag tatggcaaag gtcttgagaa tcngccattt 540  
 ggtacaaaaa aaatttttaa gcntttatgt tataccatgg aaccatagaa anggcaaggg 600  
 aattgttaag aanaatttta agtgtccaga cccanaanga aaaaaaaaaa aaaa 654

<210> 28  
 <211> 670  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (670)  
 <223> n = A,T,C or G

<400> 28  
 cgtgtgcaca tactgggagg atttccacag ctgcacgggc acagccctta cggattgcc 60

```

ggaaggggcg aaagatatgt gggataaact gagaaaagaa nccaaaaacc tcaacatcca 120
aggcagctta ttogaactct gcggcagcgg caacggggcg gcgggggtccc tgctcccggc 180
gttccccgtg ctccctgggt ctctctcggc agcttttagcg acctgncttt ccttctgagc 240
gtggggccag ctccccccgc ggcgcccacc cacnctcact ccattgctccc ggaaatcgag 300
aggaagatca ttagttcttt ggggacgttn gtgattctct gtgatgctga aaaacactca 360
tatagggaat gtgggaaatc ctganctctt tnttatntcg tntgatttct tgtgttttat 420
ttgccaaaat gttaccaatc agtgaccaac cnagcacagc caaaaatcgg acntcngctt 480
tagtccgtct tcacacacag aataagaaaa cggcaaacc accccacttt tnantttnat 540
tattactaan ttttttctgt tgggcaaaaag aatctcagga acngccctgg ggcnccgta 600
ctanagttaa ccnagctagt tncatgaaaa atgatgggct ccnctcaat gggaaagcca 660
agaaaaagnc 670

```

<210> 29

<211> 551

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(551)

<223> n = A,T,C or G

<400> 29

```

actagtcctc cacagcctgt gaatccccct agacctttca agcatagtga gcggagaaga 60
agatctcagc gtttagccac cttacccatg cctgatgatt ctgtagaaaa ggtttcttct 120
ccctctccag ccaactgatg gaaagtattc tccatcagtt ctcaaatca gcaagaatct 180
tcagtaccag aggtgcctga tgttgacat ttgccacttg agaagctggg accctgtctc 240
cctcttgact taagtcgtgg ttcagaagtt acagcaccgg tagcctcaga ttctctttac 300
cgtaatgaat gtcccagggc agaaaaagag gatacnaga tgcttccaaa tcttcttcc 360
aaagcaatag ctgatgggaa gaggagctcc agcagcagca ggaatatcga aaacagaaaa 420
aaaagtgaat ttgggaagac aaaagctcaa cagcatttgg taaggagaaa aganaagatg 480
aggaaggaag agagaagaga gacnaagatc nctacggacc gnnncggaag aagaagaagn 540
aaaaaanaaa a 551

```

<210> 30

<211> 684

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(684)

<223> n = A,T,C or G

<400> 30

```

actagttcta tctggaaaaa gcccggttg gaagaagctg tggagagtgc gtgtgcaatg 60
cgagactcat tcttggaag catccctggc aaaaatgcag ctgagtacaa ggttatcact 120
gtgatagaac ctggactgct ttttgagata atagagatgc tgcagtctga agagacttcc 180
agcacctctc agttgaatga attaatgatg gcttctgagt caactttact ggctcaggaa 240
ccacgagaga tgactgcaga tgtaatcgag cttaaaggga aattcctcat caacttagaa 300
ggtggtgata ttcgtgaaga gtcttcttat aaagtaattg tcatgccgac tacgaaagaa 360
aaatgcccc gttgttgga gtatacagcg ggagtcttca gataactgt gtcctcgatg 420
tgcagaagtt gtcagtggga aaatagtatt aacagctcac tcgagcaaga accctcctga 480
cagtactggg ctagaagttt ggatggatta tttacaatat aggaaagaaa gccaagaatt 540
aggtnatgag tggatgagta aatggtggan gatgggggaat tcaaatcaga attatggaag 600

```

aagttnttcc tggtactata gaaaggaatt atgtttatatt acatgcagaa aatatanatg 660  
 tgtgggtgtgt accgtggatg gaan 684

<210> 31  
 <211> 654  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(654)  
 <223> n = A,T,C or G

<400> 31  
 gcgcagaaaa ggaaccaata tttcagaaac aagcttaata ggaacagctg cctgtacatc 60  
 aacatcttct cagaatgacc cagaagttat catcgtggga gctggcgtgc ttggctctgc 120  
 tttggcagct gtgctttcca gagatggaag aaagggtgaca gtcattgaga gagacttaaa 180  
 agagcctgac agaatagttg gagaattcct gcagccgggt ggttatcatg ttctcaaaga 240  
 ccttggctctt ggagatacag tggaaggtct tgatgccag gttgtaaatg gttacatgat 300  
 tcatgatcag ggaaaagcaaa tcagangttc agattcctta ccctctgtca gaaaacaatc 360  
 aagtgcagag tggaagagct ttccatcacg gaagattcat catgagtctc cggaagcag 420  
 ctatggcaga gcccaatgca aagttttattg aagggtgtgt gttacagtta ttagaggaag 480  
 atgatgttgt gatgggagtt cagtacaagg ataaagagac tgggagatat caaggaactc 540  
 catgctccac tgactgttgt tgcagatggg cttttctcca anttcaggaa aagcctggtc 600  
 tcaataaagt ttctgtatca ctcatttggg tggcttctta tgaagaatgc nccc 654

<210> 32  
 <211> 673  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(673)  
 <223> n = A,T,C or G

<400> 32  
 actagtgaag aaaaagaaat tctgatacgg gacaaaaatg ctcttcaaaa catcattctt 60  
 tatcacctga caccaggagt tttcattgga aaaggatttg aacctgggtg tactaacatt 120  
 ttaaagacca cacaaggaag caaaatcttt ctgaaagaag taaatgatac acttctgggtg 180  
 aatgaattga aatcaaaaaga atctgacatc atgacaacaa atgggtgtaat tcatgttgta 240  
 gataaaactcc tctatccagc agacacacct gttggaaaatg atcaactgct ggaaatactt 300  
 aataaattaa tcaaatacat ccaaattaag tttgttcgtg gtagcacctt caaagaaatc 360  
 cccgtgactg tctatnagcc aattattaaa aaatacacca aaatcattga tgggagtgcc 420  
 tgtgggaaat aactgaaaaa gagaccgaga agaacgaatc attacagggtc ctgaaataaa 480  
 atacctagga tttctactgg aggtggagaa acagaagaac tctgaagaaa ttgttacaag 540  
 aagangtccc aaggtcacca aattcattga aggtgggtgat ggtctttatt tgaagatgaa 600  
 gaaattaaaa gacgcttcag ggagacnccc catgaaggaa ttgccagcca caaaaaaatt 660  
 cagggattag aaa 673

<210> 33  
 <211> 673  
 <212> DNA  
 <213> Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(673)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 33

actagttatt	tactttcctc	cgcttcagaa	ggtttttcag	actgagagcc	taagcatact	60
ggatctgttg	tttcttttgg	gtctcacctc	atcagtgtgc	atagtggcag	aaattataaa	120
gaaggttgaa	aggagcaggg	aaaagatcca	gaagcatggt	agttcgacat	catcatcttt	180
tcttgaagta	tgatgcatat	tgcattatgt	tatttgcaaa	ctaggaattg	cagtctgagg	240
atcattttaga	agggcaagtt	caagaggata	tgaagatttg	agaacttttt	aactattcat	300
tgactaaaaa	tgaacattaa	tgttnaagac	ttaagacttt	aacctgctgg	cagtcacaaa	360
tgaaattatg	caactttgat	atcatattcc	ttgatttaaa	ttgggctttt	gtgattgant	420
gaaactttat	aaagcatatg	gtcagttatt	tnattaaaaa	ggcaaaacct	gaaccacctt	480
ctgcacttaa	agaagtctaa	cagtacaaat	acctatctat	cttagatgga	tntatttntt	540
tntattttta	aatattgtac	tatttatggg	nggtggggct	ttcttactaa	tacacaaatn	600
aatttatcat	ttcaanggca	ttctatttgg	gtttagaagt	tgattccaag	nantgcatat	660
ttcgctactg	tnt					673

&lt;210&gt; 34

&lt;211&gt; 684

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(684)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 34

actagtttat	tcaagaaaag	aacttactga	ttcctctgtt	cctaaagcaa	gagtggcagg	60
tgatcagggc	tgggttagca	tccggttcct	ttagtgcagc	taactgcatt	tgtcactgat	120
gaccaaggag	gaaatcacta	agacatttga	gaagcagtg	tatgaacgtt	cttggacaa	180
ccacagttct	gagccttaac	cctgtagttt	gcacacaaga	acgagctcca	cctccccctt	240
ttcaggagga	atctgtgcgg	atagattggc	tggacttttc	aatggttctg	ggttgcaagt	300
gggcactggt	atggctgggt	atggagcgga	cagccccagg	aatcagagcc	tcagcccggc	360
tgcttggttg	gaaggtacag	gtgttcagca	ccttcggaaa	aagggcataa	agtngtgggg	420
gacaattctc	agtccaagaa	gaatgcattg	accattgctg	gctatttgct	tncttagtan	480
gaattggatn	catttttgac	cangatnntt	ctnctatgct	ttnttgcaat	gaaatcaaat	540
cccgatttat	ctacaagtgg	tatgaagtcc	tgcncccccc	agagaggctg	ttcaggcnat	600
gtcttccaag	ggcaggggtg	gttacaccat	tttacctccc	ctctcccccc	agattatgna	660
cncagaagga	atttntttcc	tccc				684

&lt;210&gt; 35

&lt;211&gt; 614

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(614)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 35

actagtccaa	cgcgttngcn	aatattcccc	tggtagccta	cttccttacc	cccgaatatt	60
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```

ggtaagatcg agcaatggct tcaggacatg ggttctcttc tcctgtgatc attcaagtgc 120
tactgcatg aagactggct tgtctcagtg tntcaacctc accagggctg tctcttggtc 180
cacacctgc tccctggttag tgccgtatga cagcccccat canatgacct tggccaagtc 240
acggtttctc tgtggtcaat gttggtnggc tgattggtgg aaagtanggt ggaccaaagg 300
aagnncgtg agcagncanc nccagttctg caccagcagc gcctccgtcc tactngggtg 360
ttccngtttc tcctggccct gngtgggcta nggctgatt cggaanatg cctttgcang 420
gaaggganga taantgggat ctaccaattg attctggcaa aacnatntct aagattnttn 480
tgctttatgt ggganacana tctanctctc atttntgtct gnatanaca ccctactcgt 540
gntcgancnc gtcttcgatt ttcgganaca cnccantnaa tactggcggt ctgttggttaa 600
aaaaaaaaaa aaaa 614

```

<210> 36

<211> 686

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (686)

<223> n = A,T,C or G

<400> 36

```

gtggctggcc cggttctccg cttctcccca tccctacttt tcctccctcc ctccttttcc 60
ctccctcgtc gactgttgct tgctggctgc agactccctg acccctccct caccctcccc 120
taacctcggg gccaccggat tgcccttctt ttctgttggt ccagcccagc cctagtgtca 180
gggcgggggc ctggagcagc ccgaggcact gcagcagaag ananaaaaga cacgacnaac 240
ctcagctcgc cagtccgggt gctngcttcc cgccgcagtg caatnagaca gacgccgtc 300
acctgctctg ggcacacgcg acccgtgggt gatttggcct tcagtggcat cacccttatg 360
ggtatttctt aatcagcgtc tgcaaagatg gttaacctat gctacgccag ggagatacag 420
gagactggat tggaacattt ttgggggtcta aaggtctgtt tggggtgcaa cactgaataa 480
ggatgccacc aaagcagcta cagcagctgc agatttcaca gcccaagtgt gggatgctgt 540
ctcagganat naattgataa cctggctcat aacacattgt caagaatgtg gatttcccca 600
ggatattatt atttgtttac cggggganag gataactgtt tcncntattt taattgaaca 660
aactnaaaca aaanctaagg aaatcc 686

```

<210> 37

<211> 681

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (681)

<223> n = A,T,C or G

<400> 37

```

gagacanacn naacgtcang agaanaaaag angcatggaa cacaanccag gcncgatggc 60
caccttccca ccagcancca gcgcccccca gcngccccca ngncggang accangactc 120
cancctgnat caatctganc tctattctct gcccatnctt acctcggagg tggangccgn 180
aaaggtcgca cnnncagaga agctgctgcc ancaccancc gcccnnccc tgnccggctn 240
nataggaaac tggtagccnn gctgcanaat tcatacagga gcacgcgang ggcacnnnct 300
cacactgagt tnnngatgan gcctnaccan ggacctnccc cagcnnattg annacnggac 360
tgcggaggaa ggaagacccc gnacnggatc ctggccggcn tgccaccccc ccacccttag 420
gattatnccc cttgactgag tctctgaggg gctacccgaa cccgcctcca ttccctacca 480
natnntgctc natcgggact gacangctgg ggatnggagg ggctatcccc cancatcccc 540

```

tnanaccaac	agcnacngan	natngggggt	ccccnggggtc	ggngcaacnc	tectncaccc	600
cgggcgnggc	cttcgggtgnt	gtcctcctnc	aacnaattcc	naaangggcg	gcccccngt	660
ggactcctcn	ttgttccctc	c				681

<210> 38  
 <211> 687  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(687)  
 <223> n = A,T,C or G

<400> 38						
canaaaaaa	aaaacatggc	cgaaaccagn	aagctgcgcg	atggcgccac	ggccccctctt	60
ctccccggcct	gtgtccggaa	ggtttccctc	cgaggcgccc	cggtctccgc	aagcggagga	120
gagggcgggga	cntgccgggg	ccggagctca	naggccctgg	ggccgctctg	ctctcccgcc	180
atcgcaaggg	cggcgctaac	ctnaggcctc	cccgcaaagg	tcccnangc	ggngggcgcg	240
gggggctgtg	anaaccgcaa	aaanaacgct	gggcgcgcng	cgaaccgctc	cacccccgcg	300
aaggananac	ttccacagan	gcagcgtttc	cacagcccan	agccacnttt	ctagggtgat	360
gcacccccagt	aagttcctgn	cggggaagct	caccgctgtc	aaaaaanctc	ttcgctccac	420
cggcgcacna	agggggangan	ggcangangc	tgccgcccgc	acaggtcatc	tgatcacgtc	480
gccccgcccta	ntctgtcttt	gtgaatctcc	actttgttca	accccacccg	ccgttctctc	540
ctccttgccg	cttcctctna	ccttaanaac	cagcttctc	taccnatng	tanttnctct	600
gcnenngtng	aaattaattc	ggtccnccgg	aacctcttnc	ctgtggcaac	tgctnaaaga	660
aactgctgtt	ctgnttactg	cngtccc				687

<210> 39  
 <211> 695  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(695)  
 <223> n = A,T,C or G

<400> 39						
actagtctgg	cctacaatag	tgtgattcat	gtaggacttc	tttcatcaat	tcaaaacccc	60
tagaaaaacg	tatacagatt	atataagtag	ggataagatt	tctaacattt	ctgggctctc	120
tgacccctgc	gctagactgt	ggaaagggag	tattattata	gtatacaaca	ctgctgttgc	180
cttattagtt	ataacatgat	aggtgctgaa	ttgtgattca	caatttaaaa	acactgtaat	240
ccaaactttt	ttttttaact	gtagatcatg	catgtgaatg	ttaatgttaa	tttgttcaan	300
gttgttatgg	gtagaaaaaa	ccacatgcct	taaaatttta	aaaagcaggg	cccaaactta	360
ttagtttaaa	attaggggta	tgtttccagt	ttgttattaa	ntggttatag	ctctgtttag	420
aanaaatcna	ngaacangat	ttngaaantt	aagntgacat	tatttnccag	tgacttgтта	480
atttgaaatc	anacacggca	ccttccggtt	tggtntctatt	ggnttttgaa	tccaancngg	540
ntccaaatct	tnntggaaac	ngtccnttta	acttttttac	nanatcttat	ttttttattt	600
tggaatggcc	ctattttaang	ttaaaagggg	ggggnmccac	naccattcnt	gaataaaact	660
naatatatat	ccttggtccc	ccaaaattta	aggng			695

<210> 40  
 <211> 674  
 <212> DNA



<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(674)

<223> n = A,T,C or G

<400> 40

actagtagtc agttgggagtg ggttgctata ccttgacttc atttatatga atttccactt	60
tattaaataa tagaaaagaa aatcccgggtg cttgcagtag agttatagga cattctatgc	120
ttacagaaaa tatagccatg attgaaatca aatagtaaag gctgttctgg ctttttatct	180
tcttagctca tcttaaataa gtagtacact tgggatgcag tgcgtctgaa gtgctaataca	240
gttgtaacaa tagcacaaat cgaacttagg atgtgtttct tctcttctgt gtttcgattt	300
tgatcaattc tttaatTTtg ggaacctata atacagtttt cctattcttg gagataaaaa	360
ttaaatggat cactgatatt taagtcattc tgcttctcat ctnaatattc catattctgt	420
attagganaa antacctccc agcacagccc cctctcaaac cccacccaaa accaagcatt	480
tggaaatgagt ctccttttatt tccgaantgt ggatgggtata acccatatcn ctccaatttc	540
tgnttggggtt ggggtattaat ttgaactgtg catgaaaagn ggnaatcttt nctttgggtc	600
aaanttttnc ggttaatttg nctngncaaa tccaatttnc ttttaagggtg tctttataaa	660
atttgctatt cngg	674

<210> 41

<211> 657

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(657)

<223> n = A,T,C or G

<400> 41

gaaacatgca agtaccacac actgttttgaa ttttgcacaa aaagtgactg tagggatcag	60
gtgatagccc cggaatgtac agtgtcttgg tgcaccaaga tgcttcttaa aggtgacat	120
accttggggac cctaattgggg cagagagtat agccctagcc cagtgggtgac atgaccactc	180
cctttggggag gctgaagtta aagggaatgg tatgtgtttt ctcatggaag cagcacatga	240
atnggtnaca ngatgttaaa ntaaggntct antttgggtg tcttgtcatt tgaaaaantg	300
acacactcct ancanctggg aaaggggtgc tggaagccat ggaagaactc taaaaacatt	360
agcatgggct gatctgatta cttcctggca tcccgtcac ttttatggga agtcttatta	420
naaggatggg ananttttcc atatccttgc tgttggaaact ctggaacact ctctaaattt	480
ccctctatta aaaatcactg nccttactac acttctctct tganggaata gaaatggacc	540
tttctctgac ttagttcttg gcatggganc cagcccaaatt taaaatctga cttntccggt	600
ttctccngaa ctcacctact tgaattggta aaacctcctt tggaattagn aaaaacc	657

<210> 42

<211> 389

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(389)

<223> n = A,T,C or G

<400> 42

```

actagtgtctg aggaatgtaa acaagtttgc tgggccttgc gagacttcac caggttgttt      60
cgatagctca cactcctgca ctgtgcctgt caccaggaa tgtctttttt aattagaaga      120
caggaagaaa acaaaaacca gactgtgtcc cacaatcaga aacctccgtt gtggcagang      180
ggccttcacc gccaccaggg tgtcccgcga gacagggaga gactccagcc ttctgaggcc      240
atcctgaaga attcctgttt gggggttgtg aaggaaaatc acccggtttt aaaaagatgc      300
tgttgcctgc ccgcgtngtn ggggaaggac tggtttcctg gtgaatttct taaaagaaaa      360
atattttaag ttaagaaaaa aaaaaaaaaa      389

```

```

<210> 43
<211> 279
<212> DNA
<213> Homo sapien

```

```

<400> 43
actagtgaca agtccttggg cttgagatgt cttctcgtaa aggagatggg ccttttggag      60
gtaaaggata aaatgaatga gttctgtcat gattcactat tctagaactt gcatgacctt      120
tactgtgtta gctctttgaa tgttcttgaa attttagact ttctttgtaa acaataata      180
tgtecttate attgtataaa agctgttatg tgcaacagtg tggagatcct tgtctgattt      240
aataaaatac ttaaacactg aaaaaaaaaa aaaaaaaaaa      279

```

```

<210> 44
<211> 449
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (449)
<223> n = A,T,C or G

```

```

<400> 44
actagtagca tcttttctac aacgttaaaa ttgcagaagt agcttatcat taaaaaacia      60
caacaacaac aataacaata aatcctaagt gtaaatcagt tattctaccc cctaccaagg      120
atatcagcct gttttttccc ttttttctcc tgggaataat tgtgggcttc ttcccaaatt      180
tctacagcct ctttcctctt ctcatgcttg agcttccttg tttgcacgca tgcgttgtgc      240
aagantgggc tgtttngctt ggantncggg ccnagtggaa ncatgctttc ccttgttact      300
gttgaagaa actcaaacct tcnancccta ggtgttncca ttttgtcaag tcatcactgt      360
atttttgtac tggcattaac aaaaaaagaa atnaaatatt gttccattaa actttaataa      420
aactttaaaa gggaaaaaaa aaaaaaaaaa      449

```

```

<210> 45
<211> 559
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (559)
<223> n = A,T,C or G

```

```

<400> 45
actagtgtgg gggaaatcac gacacttaaa gtcaatctgc gaaataattc ttttattaca      60
cactcactga agtttttgag tcccagagag ccattctatg tcaaacattc caagtactct      120
ttgagagccc agcattacat caacatgccc gtgcagttca aaccgaagtc cgcaggcaaa      180
tttgaagctt tgcttgtcat tcaaacagat gaaggcaaga gtattgctat tcgactaatt      240

```

ggtgaagctc	ttggaaaaaa	ttnactagaa	tactttttgt	gttaagttaa	ttacataagt	300
tgtattttgt	taactttatc	tttctacact	acaattatgc	ttttgtatat	atattttgta	360
tgatggatat	ctataattgt	agattttgtt	tttacaagct	aatactgaag	actcgactga	420
aatattatgt	atctagccca	tagtattgta	cttaactttt	acagggtgaa	aaaaaaattc	480
tgtgtttgca	ttgattatga	tattctgaat	aaatatggga	atatatttta	atgtgggtaa	540
aaaaaaaaaa	aaaaaggaa					559

&lt;210&gt; 46

&lt;211&gt; 731

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(731)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 46

actagttcta	gtaccatggc	tgtcatagat	gcaaccatta	tattccattt	agtttcttcc	60
tcaggttccc	taacaattgt	ttgaaactga	atatatatgt	ttatgtatgt	gtgtgtgttc	120
actgtcatgt	atatgggtga	tatgggatgt	gtgcagtttt	cagttatata	tatattcata	180
tatacatatg	catatatatg	tataatatac	atatatacat	gcatacactt	gtataatata	240
catatatata	cacatatatg	cacacatatn	atcactgagt	tccaaagtga	gtctttattt	300
ggggcaattg	tattctctcc	ctctgtctgc	tcactgggccc	tttgcaagac	atagcaattg	360
cttgatttcc	tttgataaag	agtcttatct	tcggcactct	tgactctagc	cttaacttta	420
gatttctatt	ccagaatacc	tctcatatct	atcttaaaac	ctaaganggg	taaagangtc	480
ataagattgt	agtatgaaag	antttgctta	gttaaattat	atctcaggaa	actcattcat	540
ctacaaatta	aattgtaaaa	tgatggtttg	ttgtatctga	aaaaatgttt	agaacaagaa	600
atgtaactgg	gtacctgtta	tatcaaagaa	cctcnattta	ttaagtctcc	tcatagccan	660
atccttatat	ngccctctct	gacctgantt	aatananact	tgaataatga	atagttaatt	720
taggnntggg	c					731

&lt;210&gt; 47

&lt;211&gt; 640

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(640)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 47

tgcgngccgg	tttggccctt	ctttgtanga	cactttcacc	cgccctgaaa	tcttcccgat	60
cgtaataaac	tcctcaggtc	cctgcctgca	caggggtttt	tcttantttg	ttgcctaaca	120
gtacaccaaa	tgtgacatcc	tttcaccaat	atngattnct	tcataccaca	tcntcnatgg	180
anacgactnc	aacaattttt	tgatnaccen	aaanactggg	ggctnnaana	agtacantct	240
ggagcagcat	ggacctgtcn	gcnactaang	gaacaanagt	nntgaacatt	tacacaacct	300
ttggtatgtc	ttactgaaag	anagaaacat	gcttctnncc	ctagaccacg	aggncaaccg	360
caganattgc	caatgccaa	tccgagcggg	tagatcaggt	aatacattcc	atggatgcat	420
tacatacntt	gtccccgaaa	nanaagatgc	cctaangget	tcttcanact	ggccngaaa	480
acanctacac	ctgggtgctg	ganaacanac	tctttggaag	atcatctggc	acaagttccc	540
cccagtgggg	tttnccttgg	cacctanctt	accanactna	ttcggaancc	attctttgcc	600
ntggcnttnt	nttgggacca	ntcttctcac	aactgnaccc			640

<210> 48  
 <211> 257  
 <212> DNA  
 <213> Homo sapien

<400> 48  
 actagtatat gaaaatgtaa atatcacttg tgtactcaaa caaaagttgg tcttaagctt 60  
 ccaccttgag cagccttgga aacctaacct gcctctttta gcataatcac attttctaaa 120  
 tgatcttctt tgttcctgaa aaagtgtatt gtattagttt tacatttggt ttttgggaaga 180  
 ttatatttgt atatgtatca tcataaaaata ttttaataaa aagtatcttt agagtgtaaa 240  
 aaaaaaaaaa aaaaaaaa 257

<210> 49  
 <211> 652  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (652)  
 <223> n = A,T,C or G

<400> 49  
 actagttcag atgagtggct gctgaagggg ccccttctgc attttcatta taacccaatt 60  
 tccacttatt tgaactctta agtcataaat gtataatgac ttatgaatta gcacagttaa 120  
 gttgacacta gaaactgccc atttctgtat tacactatca aataggaaac attggaaaga 180  
 tggggaaaaa aatcttattt taaaatggct tagaaagttt tcagattact ttgaaaattc 240  
 taaacttctt tctgtttcca aaacttgaaa atatgtagat ggactcatgc attaagactg 300  
 ttttcaaagc tttcctcaca tttttaaagt gtgattttcc ttttaataata catatttatt 360  
 ttcttttaag cagctatata ccaacccatg actttggaga tatacctatn aaaccaatat 420  
 aacagcangg ttattgaagc agctttctca aatgttgctt cagatgtgca agttgcaaat 480  
 tttattgtat ttgtanaata caatttttgt tttaaactgt atttcaatct atttctccaa 540  
 gatgcttttc atatagagtg aaatatccca ngataactgc ttctgtgtcg tcgcatttga 600  
 cgcataactg cacaaatgaa cagtgtatac ctcttggttg tgcattnacc cc 652

<210> 50  
 <211> 650  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (650)  
 <223> n = A,T,C or G

<400> 50  
 ttgcgctttg attttttttag ggcttgtgccc ctgtttcact tatagggtct agaatgcttg 60  
 tgttgagtaa aaaggagatg cccaatatcc aaagctgcta aatgttctct ttgccataaa 120  
 gactccgtgt aactgtgtga acacttggga tttttctcct ctgtcccagag gtcgtcgtct 180  
 gctttctttt ttgggttctt tctagaagat tgagaaatgc atatgacagg ctgagancac 240  
 ctcccaaac acacaagctc tcagccacan gcagcttctc cacagcccca gcttcgcaca 300  
 ggctcctgga nggctgcttg ggggaggcag acatgggagt gccaggttg ccagatgggt 360  
 ccaggactac aatgtcttta tttttaactg tttgccactg ctgcccctac cctgcccggg 420  
 ctctggagta ccgtctgccc canacaagtg ggantgaaat ggggggtgggg ggggaactg 480  
 attcccantt agggggtgcc taactgaaca gtagggtatan aaggtgtgaa cctngngaant 540

gcttttataa attatnttcc ttgttanatt tatttttttaa tttaattctct gttnaactgc 600  
ccngggaaaa ggggaaaaaa aaaaaaaaaat tctnttttaa cacatgaaca 650

<210> 51  
<211> 545  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(545)  
<223> n = A,T,C or G

<400> 51  
tggcgtgcaa ccagggtagc tgaagtttgg gtctgggact ggagattggc cattaggcct 60  
cctganattc cagctccctt ccaccaagcc cagtcttgct acgtggcaca gggcaaacct 120  
gactcccttt gggcctcagt ttccctccc cttcatgana tgaaaagaat actacttttt 180  
cttggttggtc taacnttgct ggacncaaag tgtngtcatt attggtgtat tgggtgatgt 240  
gtncaaaact gcagaagctc actgcctatg agaggaanta agagagatag tggatganag 300  
ggacanaagg agtcattatt tggatatagat ccaccntcc caacctttct ctcctcagtc 360  
cctgcncctc atgtntctgg tntggtgagt cctttgtgcc accanccatc atgctttgca 420  
ttgctgccat cctgggaagg ggggtgnatcg tctcacaact tgttgatcgc gtttganatg 480  
catgctttct tnatnaaaca aanaaannaa tgtttgacag ngttttaa at aaaaaanaaa 540  
caaaa 545

<210> 52  
<211> 678  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(678)  
<223> n = A,T,C or G

<400> 52  
actagtagaa gaactttgcc gcttttgtgc ctctcacagg cgcctaaagt cattgccatg 60  
ggaggaagac gatttggggg gggagggggg gggggcangg tccgtggggc ttccctant 120  
ntatctccat ntccantggn cnntgtegcc tcttccctcg tencattnga anttantccc 180  
tggneccenn neectctecn nectnecet cccccctcgg nencctecn cttttntan 240  
ncttccccat ctcntcccc cctnanngtc ccaacnecgn cagcaatnnc naacttnctc 300  
netecnence teennecgtt cttctnttct cnaentntnc nennntneen tgecnntnaa 360  
annetctccc cnetgcaanc gattctctcc ctecnennan ctntccactc cntncttctc 420  
nncgctect nttentenne ccactcten ccttegnecc cantacnctc neencccttn 480  
cgnntenttn nnntectenn accnecence tcccttence cctcttctcc cgggtntntc 540  
tetctecene nncnennect cnnccentec nngcgnecnt ttecgceecn cncnecntt 600  
ccttentene cantccaten cntntnecat netnecntec nctcacnccc gctnccccen 660  
ntctctttca cacngtcc 678

<210> 53  
<211> 502  
<212> DNA  
<213> Homo sapien

<220>

<221> misc\_feature  
 <222> (1)... (502)  
 <223> n = A,T,C or G

<400> 53  
 tgaagatcct ggtgtcgcca tgggcegcgc ccccgcccgt tgttacccgt attgtaagaa 60  
 caagccgtac ccaaagtctc gcttctgcgc aggtgtccct gatgcaaaa ttgcatttt 120  
 tgacctgggg cggaaaaang caaaantgga tgagtctccg ctttgtggcc acatgggtgc 180  
 agatcaatat gagcagctgt cctctgaagc cctgnanget gcccgaattt gtgccaataa 240  
 gtacatggta aaaagtngtg gcnagatgc ttccatatec ggggtgcggnt ccaccccttc 300  
 cacgtcatcc gcatcaacaa gatgttgtec tgtgtcgggg ctgacaggct cccaacaggc 360  
 atgcgaagtg cttttggaaa acccanggca ctgtggccag ggttcacatt gggccaattn 420  
 atcatgttca tccgcaccaa ctgcagaaca angaantgt naattnaagc cctgcccagg 480  
 gncaanttca aatttcccgg cc 502

<210> 54  
 <211> 494  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)... (494)  
 <223> n = A,T,C or G

<400> 54  
 actagtccaa gaaaaatatg cttaatgtat attacaaagg ctttgtatat gttaacctgt 60  
 tttaatgccaa aaagtttgct ttgtccacaa tttccttaag acctcttcag aaagggattt 120  
 gtttgccctta atgaatactg ttgggaaaaa acacagtata atgagtgaag agggcagaag 180  
 caagaaattt ctacatctta gcgactccaa gaagaatgag tatccacatt tagatggcac 240  
 attatgagga ctttaattctt tccttaaaca caataatgtt ttcttttttc ttttattcac 300  
 atgatttcta agtatatttt tcatgcagga cagtttttca accttgatgt acagtgactg 360  
 tgttaaattt ttctttcagt ggcaacctct ataactctta aaatatgggtg agcatcttgt 420  
 ctgttttgaa ngggatatga cnatnaatct atcagatggg aaatcctgtt tccaagttag 480  
 aaaaaaaaaa aaaa 494

<210> 55  
 <211> 606  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)... (606)  
 <223> n = A,T,C or G

<400> 55  
 actagtaaaa agcagcattg ccaaataatc cctaattttc cactaaaaat ataatgaaat 60  
 gatgttaagc tttttgaaaa gtttaggtta aacctactgt tgttagatta atgtatttgt 120  
 tgcttccctt tatctggaat gtggcattag cttttttatt ttaacctct ttaattctta 180  
 ttcaattcca tgacttaagg ttggagagct aaacactggg atttttggat aacagactga 240  
 cagttttgca taattataat cggcattgta catagaaagg atatggctac cttttgttaa 300  
 atctgcactt tctaaatata aaaaaaggga aatgaagtat aaatcaattt ttgtataatc 360  
 tgtttgaaac atgantttta tttgcttaat attanggctt tgcccttttc tgttagtctc 420  
 ttgggatcct gtgtaaaact gttctcatta aacaccaaac agttaagtcc attctctggt 480

actagctaca aattccgttt catattctac ntaacaattt aaattaactg aaatatttct 540  
 anatggtcta cttctgtcnt ataaaaacna aacttgantt nccaaaaaaa aaaaaaaaaa 600  
 aaaaaa 606

<210> 56  
 <211> 183  
 <212> DNA  
 <213> Homo sapien

<400> 56  
 actagtatat ttaaacttac aggcttattt gtaatgtaaa ccaccatttt aatgtactgt 60  
 aattaacatg gttataatac gtacaatcct tccctcatcc catcacacaa ctttttttgt 120  
 gtgtgataaa ctgattttgg tttgcaataa aaccttgaaa aataaaaaaa aaaaaaaaaa 180  
 aaa 183

<210> 57  
 <211> 622  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(622)  
 <223> n = A,T,C or G

<400> 57  
 actagtcact actgtcttct ccttgtagct aatcaatcaa tattcttccc ttgcctgtgg 60  
 gcagtggaga gtgctgctgg gtgtacgtg cacctgccca ctgagttggg gaaagaggat 120  
 aatcagttag cactgttctg ctcagagctc ctgatctacc ccaccacctt ggatccagga 180  
 ctgggtcaaa gctgcatgaa accaggccct ggcagcaacc tgggaatggc tggaggtggg 240  
 agagaacctg acttctcttt cctctctcct cctccaacat tactggaact ctatcctgtt 300  
 agggatcttc tgagcttgtt tccctgctgg gtgggacaga agacaaagga gaagggangg 360  
 tctacaanaa gcagcccttc tttgtcctct ggggttaatg agcttgacct ananttcag 420  
 gaganaccan aagcctctga tttttaattt centnaaatg tttgaagtnt atatntacat 480  
 atatatattt ctttnaatnt ttgagtcttt gatatgtctt aaaatccant ccctctgccn 540  
 gaaacctgaa ttaaaacct gaanaaaaat gtttncccta aagatgttan taattaattg 600  
 aaacttgaaa aaaaaaaaaa aa 622

<210> 58  
 <211> 433  
 <212> DNA  
 <213> Homo sapien

<400> 58  
 gaacaaattc tgattgggta tgtaccgtca aaagacttga agaaatttca tgattttgca 60  
 gtgtggaagc gttgaaaatt gaaagttact gcttttccac ttgctcatat agtaaaggga 120  
 tcttttcagc tgccagtgtt gaataatgta tcatccagag tgatgttatc tgtgacagtc 180  
 accagcttta agctgaacca ttttatgaat accaaataaa tagacctctt gtactgaaaa 240  
 catattttgtg actttaatcg tgctgcttgg atagaaatat ttttactggg tcttctgaat 300  
 tgacagtaaa cctgtccatt atgaatggc tactgttcta ttatttggtt tgacttgaat 360  
 ttatccacca aagacttcat ttgtgtatca tcaataaagt tgtatgtttc aactgaaaaa 420  
 aaaaaaaaaa aaa 433

<210> 59  
 <211> 649

<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)... (649)  
<223> n = A,T,C or G

<400> 59  
actagttatt atctgacttt cnggttataa tcatttctaag gagtgtgaag tagcctctgg 60  
tgtcatttgg atttgcattt ctctgatgag tgatgctatc aagcaccttt gctgggtgctg 120  
ttggccatat gtgtatgttc cctggagaag tgtctgtgct gagccttggc ccacttttta 180  
attagcgctn tgtcttttta ttactgagtt gtaaganttc tttatatatt ctggattcta 240  
gacccttata agatacatgg ttgtcaaata tttctccca ttctgtgggt tgtgttttca 300  
ctttatcgat aatgtcctta gacatataat aaatttgtat tttaaaagtg acttgatttg 360  
ggctgtgcaa ggtgggctca cgcttgtaat ccagcactt tgggagactg aggtgggtgg 420  
atcatatgan gangctagga gtctgaggtc agcctggcca gcatagcgaa aacttgtctc 480  
tacnaaaaat acaaaaatta gtcaggcatg gtgggtgcacg tctgtaatac cagcttctca 540  
ggangctgan gcacaaggat cacttgaacc ccagaangaa gangttgcag tganctgaag 600  
atcatgccag ggcaacaaaa atgagaactt gtttaaaaaa aaaaaaaaaa 649

<210> 60  
<211> 423  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)... (423)  
<223> n = A,T,C or G

<400> 60  
actagttcag gccttccagt tcaactgacaa acatggggaa gtgtgcccag ctggctggaa 60  
acctggcagt gataccatca agcctgatgt ccaaaagagc aaagaatatt tctccaagca 120  
gaagtgagcg ctgggctgtt ttagtgccag gctgcggtgg gcagccatga gaacaaaacc 180  
tcttctgtat tttttttttt cattagtana acacaagact cngattcagc cgaattgtgg 240  
tgtcttacaa ggcagggtt tcctacaggg ggtgganaaa acagcctttc ttcctttggt 300  
aggaatggcc tgagttggcg ttgtgggcag gctactgggt tgtatgatgt attagtagag 360  
caaccattta atcttttcta gtttgtatna aacttgantc gagaccttaa aaaaaaaaaa 420  
aaa 423

<210> 61  
<211> 423  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)... (423)  
<223> n = A,T,C or G

<400> 61  
cgggactgga atgtaaagtg aagttcggag ctctgagcac gggctcttcc cgccgggtcc 60  
tccctcccca gacccagag ggagaggccc accccgccc gccccgcccc agccctgtct 120  
caggtctgag tatggctggg agtcgggggc cacaggcctc tagctgtgct gctcaagaag 180



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actggatcag ggtanctaca agtggccggg ccttgccctt gggattctac cctgttcccta 240
atttggtgtt ggggtgcggg gtccctggcc cccttttcca cactncctcc ctccngacag 300
caacctccct tggggcaatt gggcctggnt ctccncccg tgttgcnacc ctttgttggt 360
ttaaggncct taaaaatgtt annttttccc ntgcnggggt taaaaaagga aaaaactnaa 420
aaa 423

```

<210> 62

<211> 683

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)... (683)

<223> n = A,T,C or G

<400> 62

```

gctggagagg ggtacggact ttcttggagt tgtcccaggt tggaatgaga ctgaactcaa 60
gaagagaccc taagagactg gggaatggtt cctgccttca ggaaagtga agacgcttag 120
gctgtcaaca cttaaaggaa gtcccttga agcccagagt ggacagacta gaccattga 180
tggggccact ggccatggc cgtggacaag acattccngt gggccatggc acaccggggg 240
ggatcaaaat gtgtacttgt ggggtctcgc cccttgccaa aaccaaacca ntccactcc 300
tgtcnttga ctttcttccc attcctcct ccccaaattgc acttcccctc ctccctctgc 360
ccctcctgtg tttttggaat tctgtttccc tcaaaattgt taatttttta nttttngacc 420
atgaacttat gtttggggtc nangttcccc ttnccaatgc atactaatat attaatggtt 480
atttattttt gaaatatttt ttaatgaact tggaaaaaat tnntggaatt tccttncttc 540
cntttntttt ggggggggtg ggggngtggg ttaaaatttt tttggaancc cnatnggaaa 600
ttnttacttg gggcccccct naaaaaantn anttccaatt cttnnatngc ccctnttccn 660
ctaaaaaaaa ananannaaa aan 683

```

<210> 63

<211> 731

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)... (731)

<223> n = A,T,C or G

<400> 63

```

actagtcata aaggggtgtgc gcgtcttcga cgtggcgggc ttggcgccac tgctgcgaga 60
cccggccctg gacctcaagg tcatccactt ggtgcgtgat ccccgcgagg tggcgagttc 120
acggatccgc tcgcgccacg gcctcctccg tgagagccta cagggtggtg gcagccgaga 180
ccgcgagctc accgcatgcc cttcttggag gccgcgggcc acaagcttgg cgcctnaaaa 240
gaaggcgtng ggggcccgc aantaccacg ctctgggcgc tatggaangt cctcttgcaa 300
taatattggt tnaaaantg canaanagcc cctgcancct cctgaactgg gntgcagggc 360
cncttacctn gtttggntgc gggtacaaag aacctgtttn ggaaaaccct nccnaaaacc 420
ttccgggaaa attntncaaa ttttnttgg ggaattnttg ggtaaaccct ccnaaaatgg 480
gaaacntttt tgccctnnaa antaaaccat tnggttcagg gggccccccc ncaaaaccct 540
ttttntttt tttntgcccc cantnncccc ccggggcccc ttttttngg ggaaaanccc 600
ccccctncc nanantttta aaaggnggg anaatttttn nttnccccc gggncccccn 660
ggngntaaaa nggtttcncc ccccgaggg gnggggnnc ctcnnaaacc cntntcnna 720
ccntttttn n 731

```

<210> 64  
 <211> 313  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(313)  
 <223> n = A,T,C or G

<400> 64  
 actagttgtg caaaccacga ctgaagaaag acgaaaagtg ggaaataact tgcaacgtct 60  
 gttagagatg gttgctacac atgttgggtc tgtagagaaa catcttgagg agcagattgc 120  
 taaagttgat agagaatatg aagaatgcat gtcagaagat ctctcggaaa atattaaaga 180  
 gattagagat aagtatgaga agaaagctac tctaattaag tcttctgaag aatgaagatn 240  
 aaatgttgat catgtatata tatccatagt gaataaaatt gtctcagtaa agttgtaaaa 300  
 aaaaaaaaaaaa aaa 313

<210> 65  
 <211> 420  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(420)  
 <223> n = A,T,C or G

<400> 65  
 actagttccc tggcaggcaa gggcttccaa ctgaggcagt gcatgtgtgg cagagagagg 60  
 caggaagctg gcagtggcag cttctgtgtc tagggagggg tgtggctccc tccttccttg 120  
 tctgggaggt tggaggggaag aatctaggcc ttagcttgcc ctctgccac ccttcccctt 180  
 gtagatactg ccttaacact cctcctctc tcagctgtgg ctgccacca agccaggttt 240  
 ctccgtgtc actaatttat ttccaggaaa ggtgtgtgga agacatgagc cgtgtataat 300  
 atttgtttta acattttcat tgcaagtatt gaccatcatc cttggttgtg tatcgttgta 360  
 acacaaatta atgatattaa aaagcatcca aacaaagccn annnnmaana nnnnnngaaa 420

<210> 66  
 <211> 676  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(676)  
 <223> n = A,T,C or G

<400> 66  
 actagtttcc tatgatcatt aaactcattc tcagggttaa gaaaggaatg taaatttctg 60  
 cctcaatttg tacttcatca ataagttttt gaagagtgcg gatttttagt caggtcttaa 120  
 aaataaactc acaaactctg atgcatttct aaattctgca aatgtttcct ggggtgactt 180  
 aacaaggaat aatcccacaa tatacctagc tacctaatac atggagctgg ggctcaaccc 240  
 actgttttta aggatttgcg cttacttggt gctgaggaaa aataagtagt tccgagggaa 300  
 gtagttttta aatgtgagct tatagatngg aaacagaata tcaacttaat tatggaaatt 360  
 gttagaaacc tgttctcttg ttatctgaat cttgattgca attactattg tactggatag 420

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actccagccc attgcaaagt ctcagatata ttanctgtgt agttgaattc cttggaaatt      480
ctttttaaga aaaaattgga gtttnaaaga aataaacccc tttgttaaat gaagcttggc      540
tttttggtga aaaanaatat tcccgcaggg cttattgttt aaaaanggaa ttttaagcct      600
ccctggaaaa anttgtaaat taaatgggga aaatgntggg naaaaattat ccggttagggt      660
ttaaaggga aactta                                     676

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<210> 67

<211> 620

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(620)

<223> n = A,T,C or G

<400> 67

```

caccattaaa gctgcttacc aagaacttcc ccagcatttt gacttccttg tttgatagct      60
gaattgtgag caggtgatag aagagccttt ctagttgaac atacagataa tttgctgaat      120
acattccatt taatgaaggg gttacatctg ttacgaagct actaagaagg agcaagagca      180
taggggaaaa aaatctgata agaacgcata aaactcacat gtgccccctc tactacaaac      240
agattgtagt gctgtggtgg tttattccgt tgtgcagaac ttgcaagctg agtcactaaa      300
cccaaagaga ggaaattata ggtagttaa acattgtaat ccaggaact aagttaatt      360
cacttttgaa gtgttttggt tttattttt ggttgtctg atttactttg ggggaaaang      420
ctaaaaaaaa agggatatca atctctaatt cagtgcccac taaaagtgtt ccctaaaaag      480
tctttactgg aanttatggg actttttaag ctccaggntt tttggtcctc caaattaacc      540
ttgcatgggc cccttaaaat tgttgaangg cattcctgcc tctaagtttg gggaaaattc      600
ccccntttt aaattttgga                                     620

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<210> 68

<211> 551

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(551)

<223> n = A,T,C or G

<400> 68

```

actagtagct ggtacataat cactgaggag ctatttctta acatgctttt atagaccatg      60
ctaattgctag accagtattt aagggttaat ctcacacctc cttagctgta agagtctggc      120
ttagaacaga cctctctgtg caataacttg tggccactgg aaatccctgg gccggcattt      180
gtattggggg tgcaatgact cccaagggcc aaaagagtta aaggcacgac tgggatttct      240
tctgagactg tggtgaaact ccttccaagg ctgagggggg cagtangtgc tctgggaggg      300
actcggcacc actttgatata tcaacaagcc acttgaagcc caattataaa attgttattt      360
tacagctgat ggaactcaat ttgaaccttc aaaactttgt tagtttatcc tattatattg      420
ttaaacctaa ttacatttgt ctagcattgg atttgggtcc tgtngcatat gtttttttcn      480
cctatgtgct cccctccccc nnatcttaat ttaaacnca attttgcnat tcncnnnnnn      540
nannnnanna a                                     551

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<210> 69

<211> 396

<212> DNA

<213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(396)  
 <223> n = A,T,C or G

<400> 69  
 cagaaatgga aagcagagtt ttcatttctg tttataaacg tctccaaaca aaaatggaaa 60  
 gcagagtttt cattaaatcc ttttaccttt tttttttctt ggtaatcccc tcaaataaca 120  
 gtatgtggga tattgaatgt taaagggata tttttttcta ttatttttat aattgtacaa 180  
 aattaagcaa atgttaaaaag ttttatatgc tttattaatg ttttcaaag gtatnataca 240  
 tgtgatacat tttttaagct tcagttgctt gtcttctggg actttctggt atgggctttt 300  
 ggggagccan aaaccaatct acnatctctt tttgtttgcc aggacatgca ataaaattta 360  
 aaaaataaat aaaaactatt nagaaattga aaaaaa 396

<210> 70  
 <211> 536  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(536)  
 <223> n = A,T,C or G

<400> 70  
 actagtgcaa aagcaaatat aaacatcgaa aaggcggtcc tcacgttagc tgaagatata 60  
 cttcgaaaga cccctgtaaa agagcccaac agtgaaaatg tagatatcag cagtggagga 120  
 ggcgtgacag gctggaagag caaatgctgc tgagcattct cctgttccat cagttgccat 180  
 ccactacccc gttttctctt cttgctgcaa aataaaccac tctgtccatt ttttaactcta 240  
 aacagatatt tttgtttctc atcttaacta tccaagccac ctattttatt tgttctttca 300  
 tctgtgactg cttgctgact ttatcataat tttcttcaaa caaaaaaatg tatagaaaaa 360  
 tcatgtctgt gaattcattt tttaatgnta cttgctcagc tcaactgcat ttcagttggt 420  
 ttatagtcca gttcttatca acattnaaac ctatngcaat catttcaaat ctattctgca 480  
 aattgtataa gaataaaagt tagaatttaa caattaaaaa aaaaaaaaaa aaaaaa 536

<210> 71  
 <211> 865  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(865)  
 <223> n = A,T,C or G

<400> 71  
 gacaaaagcgt taggagaaga anagaggcag ggaanactnc ccaggcacga tggccnctt 60  
 cccaccagca accagcgccc cccaccagcc cccaggcccc gagacgaag actccatcct 120  
 ggattaatct nacctctntc gcctgnccca ttcctacctc ggaggtggag gccggaaagg 180  
 tencaccaag aganaaactg ctgccaacac caaccgcccc agccctggcg ggcacganag 240  
 gaaactggtg accaatctgc agaattctna gaggaanaag cnagggggccc cgcgctnaga 300  
 cagagctgga tatgangcca gaccatggac nctacnccn ncaatncana cgggactgcy 360  
 gaagatggan gaccncgac nngatcaggc cngctnncca nccccccacc cctatgaatt 420  
 attcccgcgtg aangaatctc tgannggctt ccannaaagc gcctccccnc cnaacgnaan 480

tncaacatng	ggattanang	ctgggaactg	naaggggcaa	ancctnnaat	atccccagaa	540
acaanctctc	ccnaanaaac	tggggcncct	catnggtggn	accaactatt	aactaaaccg	600
cacgccaaan	aantataaaa	ggggggcccc	tcnecggngn	accccctttt	gtcccttaat	660
ganggttatc	cnccttgctg	accatggtnc	ccnnttctgt	ntgnatgttt	ccnctccctt	720
ccncctatnt	cnagccgaac	tcnnatttnc	ccgggggtgc	nacniantng	tncncctttn	780
ttngttgncc	cngccctttc	cgncggaacn	cgtttccccc	ttantaacgg	cacccggggg	840
aagggtgn	ggccccctcc	ctccc				865

&lt;210&gt; 72

&lt;211&gt; 560

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (560)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 72

cctggacttg	tcttggttcc	agaacctgac	gacccggcga	cggcgacgtc	tcttttgact	60
aaaagacagt	gtccagtgtc	ccngcctagg	agtctacggg	gaccgcctcc	cgcgccgcca	120
ccatgcccaa	cttctctggc	aactggaaaa	tcatccgac	ggaaaacttc	gangaattgc	180
tcnaantgct	gggggtgaat	gtgatgctna	ngaanattgc	tgtggctgca	gcgtccaagc	240
cagcagtggg	gatcnaacag	gaggagagaca	ctttctacat	caaaacctcc	accaccgtgc	300
gcaccacaaa	gattaacttc	nnngttgggg	aggantttga	ggancaaact	gtggatngga	360
ngcctgtnaa	aacctggtga	aatgggagaa	tganaataaa	atggtctgtg	ancanaaact	420
cctgaaayga	gaaggcccc	anaactcctg	gaccngaaaa	actgaccnc	cnatngggga	480
actgatnctt	gaacctgaa	cgggcgggat	ganccttttt	tnttgccncc	naanggggtc	540
tttccntttc	cccaaaaaaa					560

&lt;210&gt; 73

&lt;211&gt; 379

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (379)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 73

ctggggganc	ggcggtnnge	nccatntcnn	gncgcgaagg	tggcaataaa	aancnctga	60
aaccgcncaa	naaacatgcc	naagatatgg	acgaggaaga	tngngctttc	nngnacaanc	120
gnannagga	acanaacaaa	ctcnangagc	tctcaagcta	atgccgcggg	gaagggggcc	180
ttggccacnn	gtggaattaa	gaaatctggc	aaanngtann	tgttccttgt	gcctnangag	240
ataagngacc	ctttatttca	tctgtattta	aacctctctn	ttccctgnca	taacttcttt	300
tnccacgtan	agntggaant	anttggtgtc	ttggactgtt	gtncatttta	gannaaactt	360
ttgttcaaaa	aaaaaataa					379

&lt;210&gt; 74

&lt;211&gt; 437

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

<221> misc\_feature  
 <222> (1) ... (437)  
 <223> n = A,T,C or G

<400> 74  
 actagttcag actgccacgc caaccccaga aaatacccca catgccagaa aagtgaagtc 60  
 ctaggtgttt ccatctatgt ttcaatctgt ccatctacca ggccctcgca taaaaacaaa 120  
 acaaaaaaac gctgccaggt ttanaagca gttctggctc caaaaccatc aggatcctgc 180  
 caccagggtt cttttgaaat agtaccacat gtaaaaggga atttggcttt cacttcatct 240  
 aatcactgaa ttgtcaggct ttgattgata attgtagaaa taagtagcct tctgttgtgg 300  
 gaataagtta taatcagtat tcatctcttt gttttttgtc actcttttct ctctnattgt 360  
 gtcatttgta ctgtttgaaa aatattttct ctataaaatt aaactaacct gccttaaaaa 420  
 aaaaaaaaaa aaaaaaa 437

<210> 75  
 <211> 579  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (579)  
 <223> n = A,T,C or G

<400> 75  
 ctccgtcgcc gccaaagatga tgtgcggggc gccctccgcc acgcagccgg ccaccgcga 60  
 gaccagcac atcgccgacc aggtgaggtc ccagcttgaa gagaaagaaa acaagaagtt 120  
 cctgtgttt aaggccgtgt cattcaagag ccagggtggtc ggggggacaa actacttcat 180  
 caagggtcac gtcggcgacg aggacttcgt acacctgcga gtgttccaat ctctccctca 240  
 tgaaaacaag cccttgacct tatctaacta ccagaccaac aaagccaagc atgatgagct 300  
 gacctatttc tgatcctgac ttgggacaag gcccttcagc cagaagactg acaaagtcac 360  
 cctccgtcta ccagagcgtg cacttgtgat cctaaaataa gcttcatctc ogggctgtgc 420  
 ccttgggggtg gaaggggcan gatctgcact gcttttgcac ttctcttctt aaatttcatt 480  
 gtgttgattc ttctcttcca ataggtgac ttnattactt tcagaatatt ttccaaatna 540  
 gatattttt naaaatcctt aaaaaaaaaa aaaaaaaaaa 579

<210> 76  
 <211> 666  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (666)  
 <223> n = A,T,C or G

<400> 76  
 gtttatecta tctctccaac cagattgtca gctccttgag ggcaagagcc acagtatatt 60  
 tccctgtttc ttccacagtg cctaataata ctgtggaact aggttttaata aatttttta 120  
 ttgatgttgt tatgggcagg atggcaacca gaccattgtc tcagagcagg tgctggctct 180  
 ttctggcta ctccatgttg gctagcctct ggtaacctct tacttattat cttcaggaca 240  
 ctactacag ggaccaggga tgatgcaaca tccttgtctt tttatgacag gatgtttgct 300  
 cagcttctcc aacaataaaa agcacgtggt aaaacacttg cggatattct ggactgtttt 360  
 taaaaatat acagtttacc gaaaatcata ttatcttaca atgaaaagga ntttatagat 420  
 cagccagtga acaacctttt cccaccatac aaaaattcct tttcccgaan gaaaanggct 480

ttctcaataa	ncctcacttt	cttaanatct	tacaagatag	ccccganatc	ttatcgaaac	540
tcatttttagg	caaatatgan	ttttattgtg	cgttacttgt	ttcaaaattt	gggtattgtga	600
atatcaatta	ccacccccat	ctcccatgaa	anaaaangga	aanggtgaan	ttcntaanng	660
cttaaa						666

<210> 77  
 <211> 396  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (396)  
 <223> n = A,T,C or G

ctgcagcccg	ggggatccac	taatctacca	nggttatttg	gcagctaatt	ctanatttgg	60
atcattgccc	aaagtgtcac	ttgctgggtc	cttgggattt	ggccttggaa	aggtatcata	120
catanganta	tgccanaata	aattccattt	ttttgaaaat	canctccntg	gggctgggtt	180
tggtccacag	cataacangc	actgcctcct	tacctgtgag	gaatgcaaaa	taaagcatgg	240
attaagttag	aaggagagact	ctcagccttc	agcttccctaa	attctgtgtc	tgtgactttc	300
gaagtttttt	aaacctctga	atttgtacac	atttaaaatt	tcaagtgtac	tttaaaataa	360
aatacttcta	atgggaacaa	aaaaaaaaaa	aaaaaa			396

<210> 78  
 <211> 793  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (793)  
 <223> n = A,T,C or G

gcatectagc	cgccgactca	cacaaggcag	gtgggtgagg	aaatccagag	ttgccatgga	60
gaaaattcca	gtgtcagcat	tcttgctcct	tgtggccctc	tcctacactc	tgccagaga	120
taccacagtc	aaacctggag	ccaaaaagga	cacaaaggac	tctcgaccca	aactgcccc	180
gacctctctc	agaggttggg	gtgaccaact	catctggact	cagacatatg	aagaagctct	240
atataaatcc	aagacaagca	acaaaccctt	gatgattatt	catcacttgg	atgagtggcc	300
acacagtcna	gctttaaaga	aagtgtttgc	tgaaaataaa	gaaatccaga	aattggcaga	360
gcagtttgtc	ctcctcaatc	tggtttatga	aacaactgac	aaacaccttt	ctcctgatgg	420
ccagtatgtc	ccaggattat	gtttgttgac	ccatctctga	cagttgaagc	cgatatcctg	480
ggaagatatt	cnaaccgtct	ctatgcttac	aaactgcaga	tacgctctgt	tgcttgacac	540
atgaaaaagc	tctcaagttg	ctnaaaatga	attgtaagaa	aaaaaatctc	cagccttctg	600
tctgtcggct	tgaaaattga	aaccagaaaa	atgtgaaaaa	tggctattgt	ggaacanatn	660
gacacctgat	taggttttgg	ttatgttcac	cactattttt	anaaaanan	nttttaaaat	720
ttggttcaat	tntctttttn	aaacaatntg	tttctacntt	gnganctgat	ttctaaaaaa	780
aataatnttt	ggc					793

<210> 79  
 <211> 456  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(456)  
 <223> n = A,T,C or G  
  
 <400> 79  
 actagtatgg ggtgggaggc cccacccttc tcccctaggc gctgttcttg ctccaaaggg 60  
 ctccgtggag agggactggc agagctgang ccacctgggg ctggggatcc cactcttctt 120  
 gcagctgttg agcgcaccta accactgggc atgccccac cctgctctc cgcacccgct 180  
 tcctcccgac cccangacca ggctacttct cccctcctct tgccctccctc ctgcccctgc 240  
 tgccctctgat cgtangaatt gangantgtc ccgccttgtg gctganaatg gacagtggca 300  
 ggggctggaa atgggtgtgt gtgtgtgtgt gtgtgtgtgt gtgtgtgtgt gcnccccccc 360  
 tgcaagaccg agattgaggg aaancatgtc tgctgggtgt gaccatgttt cctctccata 420  
 aantnccct gtgacnctca naaaaaaaaa aaaaaa 456

<210> 80  
 <211> 284  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(284)  
 <223> n = A,T,C or G

<400> 80  
 ctttgtacct ctagaaaaga taggtattgt gtcatgaaac ttgagttaa attttatata 60  
 taaaactaaa agtaatgtc actttagcaa cacatactaa aattggaacc atactgagaa 120  
 gaatagcatg acctccgtgc aaacaggaca agcaaatttg tgatgtgttg attaaaaaga 180  
 aataaataaa tgtgtatatg tgtaacttgt atgtttatgt ggaatacaga ttgggaaata 240  
 aaatgtattt cttactgtga aaaaaaaaaa aaaaaaaaaa aana 284

<210> 81  
 <211> 671  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(671)  
 <223> n = A,T,C or G

<400> 81  
 gccaccaaca ttccaagcta ccctgggtac ctttgtgcag tagaagctag tgagcatgtg 60  
 agcaagcggg gtgcacacgg agactcatcg ttataattta ctatctgcca agagtagaaa 120  
 gaaaggctgg ggatatattg gttggcttgg ttttgatttt ttgcttgttt gtttgttttg 180  
 tactaaaaca gtattatctt ttgaatatcg tagggacata agtatataca tgttatccaa 240  
 tcaagatggc tagaatgggtg cctttctgag tgtctaaaac ttgacacccc tggtaaattct 300  
 ttcaacacac ttccactgcc tgcgtaatga agttttgatt catttttaac cactggaatt 360  
 tttcaatgcc gtcattttca gttagatnat tttgcacttt gagattaaaa tgccatgtct 420  
 atttgattag tcttattttt ttatttttac aggcttatca gtctcactgt tggctgtcat 480  
 tgtgacaaaag tcaaataaac ccccnaggac aacacacagt atgggatcac atattgtttg 540  
 acattaagct ttggccaaaa aatgttgcac gtgttttacc tcgacttgct aaatcaatan 600  
 canaaaggct ggctnataat gttgggtggtg aaataattaa tnantaacca aaaaaaaaaa 660  
 aaaaaaaaaa a 671



<210> 82  
 <211> 217  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (217)  
 <223> n = A,T,C or G

<400> 82  
 ctgcagatgt ttcttgaatg ctttgtcaaa ttaanaaagt taaagtgcaa taatgtttga 60  
 agacaataag tgggtggtgta tcttgtttct aataagataa acttttttgt ctttgcttta 120  
 tcttattagg gagttgtatg tcagtgtata aaacatactg tgtggtataa caggcttaat 180  
 aaattcttta aaaggaaaaa aaaaaaaaaa aaaaaaa 217

<210> 83  
 <211> 460  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (460)  
 <223> n = A,T,C or G

<400> 83  
 cgcgagtggg agcaccagga tctcgggctc ggaacgagac tgcacggatt gttttaagaa 60  
 aatggcagac aaaccagaca tgggggaaat cgccagcttc gatnaggcca agctgaanaa 120  
 aacggagacg caggagaaga acaccctgcc gaccaaagag accattgagc angagaagcg 180  
 gagtgaaatt tctaagatc ctggaggatt tctaccccc gtcctcttcg agacccagct 240  
 cgtgatgtgg aggaagagcc acctgcaaga tggacacgag ccacaagctg cactgtgaac 300  
 ctgggcactc cgcgccgatg ccaccggcct gtgggtctct gaagggaccc cccccaatcg 360  
 gactgccaaa ttctccggtt tgccccggga tattatacaa nattatttgt atgaataatg 420  
 annataaaac acacctcgtg gcancaana aaaaaaaaaa 460

<210> 84  
 <211> 323  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (323)  
 <223> n = A,T,C or G

<400> 84  
 tgggtgatct tggctctgtg gagctgctgg gacgggatct aaaagactat tctggaagct 60  
 gtggtccaan gcattttgct ggcttaacgg gtcccgaac aaaggacacc agctctctaa 120  
 aattgaagtt taccoganat aacaatcttt tgggcagaga tgctattttt aacaaacncc 180  
 gtccctgcgc aacaacnaac aatctctggg aaataccggc catgaacntg ctgtctcaat 240  
 cnancatctc tctagctgac cgatcatatc gtcccagatt actacanatc ataataattg 300  
 atttctctgta naaaaaaaaaa aaa 323

<210> 85  
 <211> 771  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(771)  
 <223> n = A,T,C or G

<400> 85  
 aaactgggta ctcaacactg agcagatctg ttctttgagc taaaaaccat gtgctgtacc 60  
 aanagtttgc tcttggctgc tttgatgtca gtgctgtac tccacctctg cggcgaatca 120  
 gaagcaagca actttgactg ctgtcttgga tacacagacc gtattcttca tcctaaattt 180  
 attgtgggct tcacacggca gctggccaat gaaggctgtg acatcaatgc tatcatcttt 240  
 cacacaaaga aaaagttgtc tgtgtgcgca aatccaaaac agacttgggt gaaatatatt 300  
 gtgcgtctcc tcagtaaaaa agtcaagaac atgtaaaaac tgtggctttt ctggaatgga 360  
 attggacata gcccaagaac agaaagaact tgctgggggt ggagggttca cttgcacatc 420  
 atgganggtt tagtgcttat cttatttctg cctcctggac ttgtccaatt natgaagtta 480  
 atcatattgc atcatanttt gctttgttta acatcacatt naaattaaac tgtattttat 540  
 gttatttata gctntagggt ttctgtgttt aactttttat acnaantttc ctaaactatt 600  
 ttggtntant gcaanttaaa aatttatatt ggggggggaa taaatattgg antttctgca 660  
 gccacaagct ttttttaaaa aaccantaca nccnngttaa atggtnggtc ccnaatgggt 720  
 tttgcttttn antagaaaat ttnttagaac natttgaaaa aaaaaaaaaa a 771

<210> 86  
 <211> 628  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(628)  
 <223> n = A,T,C or G

<400> 86  
 actagtttgc tttacatttt tgaaaagtat tatttttgtc caagtgttta tcaactaaac 60  
 cttgtgttag gtaagaatgg aattttattaa gtgaatcagt gtgaccttc ttgtcataag 120  
 attatcttaa agctgaagcc aaaatatgct tcaaaagaaa angactttat tgttcattgt 180  
 agttcataca ttcaaagcat ctgaactgta gtttctatag caagccaatt acatccataa 240  
 gtggagaang aaatagatta atgtcnaagt atgattgggt gagggagcaa gggtgaagat 300  
 aatctgggggt tgaaattttc tagttttcat tctgtacatt tttagttna catcagattt 360  
 gaaatattaa tgtttacctt tcaatgtgtg gtatcagctg gactcantaa caccctttc 420  
 ttccctnnggg gatggggaat ggattattgg aaaatggaaa gaaaaaagta cttaaagcct 480  
 tcctttcnca gtttctggct cctaccctac tgatttancc agaataagaa aacattttat 540  
 catcntctgc tttattccca ttaatnaant tttgatgaat aaatctgctt ttatgcnnac 600  
 ccaaggaatt nagtggnttc ntcnttgt 628

<210> 87  
 <211> 518  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature

&lt;222&gt; (1) ... (518)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 87

ttttttat	tttttagaga	gtagttcagc	ttttat	aaatttattg	cctgttttat	60
tataacaaca	ttatactggt	tatggtttaa	tacatatggt	tcaaaatgta	taatacatca	120
agtagtacag	ttttaaaatt	ttatgcttaa	aacaagtttt	gtgtaaaaaa	tgcagatata	180
ttttacatgg	caaatcaatt	tttaagtcac	cctaaaaatt	gatttttttt	tgaaatttaa	240
aaacacattt	aatttcaatt	tctctcttat	ataaccttta	ttactatagc	atggtttcca	300
ctacagttta	acaatgcagc	aaaattccca	tttcacggta	aattggggtt	taagcggcaa	360
ggttaaaatg	ctttgaggat	cctnaatacc	ctttgaactt	caaatgaagg	ttatggttgt	420
naatttaacc	ctcatgccat	aagcagaagc	acaagtttag	ctgcattttg	ctctaaactg	480
taaaancgag	ccccccgttg	aaaaagcaaa	agggaccc			518

&lt;210&gt; 88

&lt;211&gt; 1844

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 88

gagacagtga	atcctagtat	caaaggattt	ttggcctcag	aaaaagttgt	tgattat	60
tattttat	tatttttcga	gactcogtct	caaaaaaaaa	aaaaaaaaaa	agaatcacia	120
ggtagttgct	aaagcatf	gagctgcttg	gaaaaaggga	agtagttgca	gtagagtttc	180
ttccatcttc	ttgggtgctgg	gaagccatat	atgtgtcttt	tactcaagct	aaggggtata	240
agcttatgtg	ttgaatttgc	tacatctata	tttcacatat	tctcacaata	agagaatttt	300
gaaatagaaa	tatcatagaa	catttaagaa	agtttagtat	aaataatatt	ttgtgtgttt	360
taatcccttt	gaagggatct	atccaaagaa	aatattttac	actgagctcr	ttcctacacg	420
tctcagtaac	agatcctgtg	ttagtctttg	aaaatagctc	attttttaaa	tgtcagttag	480
tagatgtagc	atacatatga	tgtataatga	cgtgtattat	gttaacaatg	tctgcagatt	540
ttgtaggaat	acaaaacatg	gcctttttta	taagcaaaac	gggccaatga	ctagaataac	600
acatagggca	atctgtgaat	atgtattata	agcagcattc	cagaaaagta	gttggtgaaa	660
taattttcaa	gtcaaaaagg	gatatggaaa	gggaattatg	agtaacctct	attttttaag	720
ccttgctttt	aaattaaacg	ctacagccat	ttaagccttg	aggataataa	agcttgagag	780
taataatgtt	aggttagcaa	aggttttagat	gtatcacttc	atgcatgcta	ccatgatagt	840
aatgcagctc	ttcagatcat	ttctgggtcat	tcaagatatt	cacctttttg	cccatagaaa	900
gcacctacc	tcacctgctt	actgacattg	tcttagctga	tcacaagatc	attatcagcc	960
tccattat	cttactgtat	ataaaataca	gagttttata	ttttcctttc	ttcgtttttc	1020
accatattca	aaacctaaat	ttgtttttgc	agatggaatg	caaagtaatc	aagtgttcgt	1080
gctttcacct	agaagggtgt	ggctcctgaag	gaaagaggtc	cctaaatatc	ccccacctg	1140
ggtagctctc	cttccctggg	accctgacta	ccagaagtca	ggtagctagag	cagctggaga	1200
agtgcagcag	cctgtgcttc	cacagatggg	ggtagctgctg	caacaaggct	ttcaatgtgc	1260
ccatcttagg	gggagaagct	agatcctgtg	cagcagcctg	gtaagtcctg	aggaggttcc	1320
attgctcttc	ctgctgctgt	cctttgcttc	tcaacggggc	tcgctctaca	gtctagagca	1380
catgcagcta	acttgtgcct	ctgcttatgc	atgagggtta	aattaacaac	cataaccttc	1440
atltgaagtt	caaagggtga	ttcaggatcc	tcaaagcatt	ttaaccttgc	cgcttaaaac	1500
ccaatttacc	gtgaaatggg	aattttgctg	cattgttaaa	ctgtagtgga	aaccatgcta	1560
tagtaataaa	ggttatataa	gagagaaatt	gaaattaaat	gtgtttttta	atttcaaaaa	1620
aaaatcaatc	tttaggatga	cttaaaaatt	gatttgccat	gtaaaatgta	tctgcatttt	1680
ttacacaaaa	cttgttttta	gcataaaatt	ttaaaactgt	actacttgat	gtattatata	1740
ttttgaacca	tatgtattaa	accataaaca	gtataatgtt	gttataataa	aacaggcaat	1800
aaatttataa	ataaaagctg	aaaaaaaaaa	aaaaaaaaaa	aaaa		1844

&lt;210&gt; 89

&lt;211&gt; 523

&lt;212&gt; DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(523)

<223> n = A,T,C or G

<400> 89

tttttttttt	tttttttagt	caatccacat	ttattgatca	cttattatgt	accaggcact	60
gggataaaga	tgactgttag	tcactcacag	taaggaagaa	aactagcaaa	taagacgatt	120
acaatatgat	gtagaaaatg	ctaagccaga	gatatagaaa	ggtcctattg	ggtccttctg	180
tcacctgtgc	tttccacatc	cctacccttc	acaggccttc	cctccagctt	cctgcccccg	240
ctccccactg	cagatccccct	gggattttgc	ctagagctaa	acgagganat	gggccccctg	300
gccctggcat	gacttgaacc	caaccacaga	ctgggaaagg	gagcctttcg	anagtggatc	360
actttgatna	gaaaacacat	aggggaattga	agagaaantc	cccaaattggc	cacccgtgct	420
ggtgctcaag	aaaagtttgc	agaatggata	aatgaaggat	caagggaatt	aatanatgaa	480
taattgaatg	gtggctcaat	aagaatgact	ncnttgaatg	acc		523

<210> 90

<211> 604

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(604)

<223> n = A,T,C or G

<400> 90

ccagtgtggt	ggaatgcaaa	gattacccccg	gaagcttttcg	agaagctggg	attccctgca	60
gcaaaggaaa	tagccaatat	gtgtcgtttc	tatgaaatga	agccagaccg	agatgtcaat	120
ctcaccacc	aactaaatcc	caaagtcaaa	agcttcagcc	agtttatctc	agagaaccag	180
gggagccttc	aagggcatgt	agaaaatcag	ctgttcagat	aggcctctgc	accacacagc	240
ctctttcctc	tctgatcctt	ttcctcttta	cggcacaaca	ttcatgtttg	acagaacatg	300
ctggaatgca	attgtttgca	acaccgaagg	atttcctgcg	gtcgccctctt	cagtaggaag	360
cactgcattg	gtgataggac	acggtaattt	gattcacatt	taacttgcta	gttagtgata	420
aggggtggta	cacctgtttg	gtaaaatgag	aagcctcgga	aacttgggag	cttctctcct	480
accactaatg	gggagggcag	attattactg	ggattttctcc	tggggtgaat	taatttcaag	540
ccctaattgc	tgaaattccc	ctnggcaggc	tccagttttc	tcaactgcat	tgcaaaattc	600
cccc						604

<210> 91

<211> 858

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(858)

<223> n = A,T,C or G

<400> 91

tttttttttt	ttttttttta	tgattattat	tttttttatt	gatctttaca	tcctcagtg	60
tggcagagtt	tctgatgctt	aataaacatt	tgttctgatc	agataagtgg	aaaaaattgt	120
catttcctta	ttcaagccat	gcttttctgt	gatattctga	tcctagttga	acatacagaa	180

ataaatgtct	aaaacagcac	ctcgattctc	gtctataaca	ggactaagtt	cactgtgac	240
ttaaataagc	ttggctaaaa	tgggacatga	gtggaggtag	tcacacttca	gcgaagaaag	300
agaatctcct	gtataatctc	accaggagat	tcaacgaatt	ccaccacact	ggactagtgg	360
atcccccg	ctgcaggaat	tcgatatcaa	gcttatcgat	accgtcgacc	tcgagggggg	420
gccccgtacc	caattcgccc	tatagttagt	cgtattacgc	gcgctcactg	gccgtcgttt	480
tacaacgtcg	tgactgggaa	aaccctggcg	ttaccecaact	taatcgccct	gcagcacatc	540
cccctttcgc	cagctggcgt	aatagcgaan	agccccgacc	gacgcgccct	ncaacagttg	600
cgcagcctga	atggcgaatg	ggacgcgccc	tgtagcggcg	cattaaagcg	cggcnggggtg	660
tggnggntcc	cccacgtgac	cgntacactt	ggcagcgccct	tacgcgggtc	nttcgctttc	720
ttcccttccct	ttctcgaccc	gttcgcgggg	tttccccggn	agctnttaat	cgggggnctc	780
cctttanggg	tncnaattaa	nggnttacng	gacctnngan	cccaaaaact	ttgattaggg	840
ggaaggtccc	cgaagggg					858

&lt;210&gt; 92

&lt;211&gt; 585

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (585)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 92

gttgaatctc	ctggtgagat	tatacaggag	attctctttc	ttcgtgaag	tgtgactacc	60
tccactcatg	tcccatttta	gccaagctta	tttaagatca	cagtgaactt	agtcctgtta	120
tagacgagaa	tcgaggtgct	gttttagaca	tttatctctg	tatgttcaac	taggatcaga	180
atatcacaga	aaagcatggc	ttgaataagg	aaatgacaat	tttttccact	tatctgatca	240
gaacaaatgt	ttattaagca	tcagaaactc	tgccaacact	gaggatgtaa	agatcaataa	300
aaaaaataat	aatcatnann	naaanannan	nngaaggcg	gccgccaccg	cgggtggagct	360
ccagcttttg	ttcccttttag	tgaggggttaa	ttgcgcgctt	ggcgttaatc	atggtcatag	420
ctgtttccctg	tgtgaaattg	ttatccggct	cacaattccn	cncaacatac	gagccgggaa	480
gcntnangtg	taaaagcctg	gggggtgccta	attgagtgag	ctnactcaca	ttaattgngt	540
tgcgctccac	ttgcccgcctt	ttccantccg	ggaaacctgt	tcgnc		585

&lt;210&gt; 93

&lt;211&gt; 567

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (567)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 93

cggcagtggt	gctgtctgcg	tgtccacctt	ggaatctggc	tgaactggct	gggaggacca	60
agactgcggc	tgggggtggc	anggaaggga	accgggggct	gctgtgaagg	atcttggaac	120
ttccctgtac	ccaccttccc	cttgcttcat	gtttgtanag	gaaccttggt	ccggccaagc	180
ccagtttccct	tgtgtgatac	actaatgtat	ttgctttttt	tgggaaatan	anaaaaaatca	240
attaaattgc	tantgtttct	ttgaannnnn	nnnnnnnnnn	nnnnnnnggg	ggggncgccc	300
ccnccgngga	aacnccccct	ttgttccctt	ttaattgaaa	ggttaattng	cncncntggc	360
gttaancnt	gggccaaanc	tngttncccg	tgntgaaatt	gttnatcccc	tcccaaatc	420
ccccccncc	ttccaaaccc	ggaaancctn	annntgttna	ancccggggg	gttgccctaan	480
ngnaattnaa	ccnaaccccc	ntttaaatng	nnnttgcncn	ccacnngccc	cncctttccca	540

nttcgggggaa aaccctntcc gtgcccc

567

<210> 94  
 <211> 620  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(620)  
 <223> n = A,T,C or G

<400> 94  
 actagtcaaa aatgctaaaa taatttggga gaaaatattt ttaagtagt gttatagttt 60  
 catgtttatc ttttattatg ttttgtgaag ttgtgtcttt tcactaatta cctatactat 120  
 gccaatatct ccttatatct atccataaca ttatactac atttgtaana naatatgcac 180  
 gtgaaactta acactttata aggtaaaaat gaggtttcca anatttaata atctgatcaa 240  
 gttcttggtta ttccaaata gaatggactt ggtctgttaa gggctaagga gaagaggaag 300  
 ataagggttaa aagttgttaa tgaccaaaca ttctaaaaga aatgcaaaaa aaaagtttat 360  
 tttcaagcct tcgaactatt taaggaaagc aaaatcattt cctaaatgca tatcatttgt 420  
 gagaatttct cattaatatc ctgaatcatt catttcacta aggctcatgt tnactccgat 480  
 atgtctctaa gaaagtacta tttcatggtc caaacctggg tgccatantt gggtaaaggc 540  
 tttcccttaa gtgtgaaant atttaaaatg aaattttcct ctttttaaaa attctttana 600  
 aggggttaagg gtgttgggga 620

<210> 95  
 <211> 470  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(470)  
 <223> n = A,T,C or G

<400> 95  
 ctgcaccttc tctgcacagc ggatgaaccc tgagcagctg aagaccagaa aagccactat 60  
 nactttntgc ttaattcang agcttacang attcttcaaa gagtgngtcc agcatccttt 120  
 gaaacatgag ttcttaccag cagaagcaga cctttacccc accacctcag cttcaacagc 180  
 agcaggtgaa acaacccatc cagcctccac ctnaggaaat atttggtccc acaaccaagg 240  
 agccatgcca ctcaaagggt ccacaacctg naaacacaaa nattccagag ccaggctgta 300  
 ccaagggtccc tgagccaggg ctgtaccaan gtccctgagc cagggtgtac caangtcctt 360  
 gagccaggat gtaccaagggt ccctgancca gggtgtccaa ggtccctgag ccaggctaca 420  
 ccaagggcct gngccaggca gcatcaangt ccctgaccaa ggcttatcaa 470

<210> 96  
 <211> 660  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(660)  
 <223> n = A,T,C or G

```

<400> 96
tttttttttt tttttttttt ggaattaaaa gcaatttaat gagggcagag caggaaacat      60
gcatttcctt tcattogaat cttcagatga accctgagca gccgaagacc agaaaagcca      120
tgaagacttt ctgcttaatt caggggctta caggattctt cagagtgtgt gtgaacaaaa      180
gctttatagt acgtattttt aggatacaaa taagagagag actatggctt ggggtgagaa      240
tgtactgatt acaaggtcta cagacaatta agacacagaa acagatggga agagggtgnc      300
cagcatctgg nggttggtct ctcaagggtt tgtctgtgca ccaaattact tctgcttggn      360
cttctgctga gctgggcctg gagtgaccgt tgaaggacat ggctctggta cctttgtgta      420
gcctgncaca ggaactttgg tgtatccttg ctcaggaaact ttgatggcac ctggctcagg      480
aaacttgatg aagccttggt caagggaact tgatgcttgc tggctcaggg accttggnn      540
ancctgggct canggacctt tgnncnaacc ttggcttcaa gggacccttg gnacatcctg      600
gcnnagggac ccttggnncc aacctggggc ttnagggacc ctttggnnnc nancctgggc      660

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<210> 97

<211> 441

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (441)

<223> n = A,T,C or G

```

<400> 97
gggaccatac anagtattcc tctcttcaca ccaggaccag ccactgttgc agcatgagtt      60
cccagcagca gaagcagccc tgcacccac ccctcagct tcagcagcag caggtgaaac      120
agccttgcca gcctccacct caggaaccat gcatcccca aaccaaggag ccctgccacc      180
ccaaggtgcc tgagccctgc caccctaaag tgccctgagcc ctgccagccc aaggttccag      240
agccatgcca cccaaggtg cctgagccct gcccttcaat agtcactcca gcaccagccc      300
agcagaanac caagcagaag taatgtggtc cacagccatg cccttgagga gccggccacc      360
agatgctgaa tccctatcc cattctgtgt atgagtccca tttgccttgc aattagcatt      420
ctgtctcccc caaaaaaaaa a                                     441

```

<210> 98

<211> 600

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (600)

<223> n = A,T,C or G

```

<400> 98
gtattcctct cttcacacca ggaccagcca ctgttgccgc atgagttccc agcagcagaa      60
gcagccctgc atcccacccc ctcagcttca gcagcagcag gtgaaacagc cttgccagcc      120
tccacctcag gaaccatgca tccccaaaac caaggagccc tgccacccca aggtgcctga      180
gccctgccac cccaaagtgc ctgagccctg ccagcccaag gttccagagc catgccacc      240
caaggtgcct gagccctgcc cttcaatagt cactccagca ccagcccagc agaanaccaa      300
gcagaagtaa tgtggtccac agccatgccc ttgaggagcc ggccaccana tgctgaatcc      360
cctatcccat tctgtgtatg agtcccattt gccttgcaat tagcattctg tctcccccaa      420
aaaagaatgt gctatgaagc tttctttcct acacactctg agtctctgaa tgaagctgaa      480
ggctttaant acaganctag ttttcagctg ctcagaattc tctgaagaaa agatttaaga      540
tgaaaggcaa atgattcagc tccttattac cccattaaat tcnctttcaa ttccaaaaaa      600

```

<210> 99  
 <211> 667  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (667)  
 <223> n = A,T,C or G

<400> 99  
 actagtgact gagttcctgg caaagaaatt tgacctggac cagttgataa ctcattgtttt 60  
 accattttaa aaaatcagtg aaggatttga gctgctcaat tcaggacaaa gcattcgaac 120  
 ggtcctgacg ttttgagatc caaagtggca ggaggtctgt gttgtcatgg tgaactggag 180  
 tttctcttgt gagagttccc tcatctgaaa tcatgtatct gtctcacaaa tacaagcata 240  
 agtagaagat ttgttgaaaga catagaaccc ttataaagaa ttattaacct ttataaacat 300  
 tttaaagtctt gtgagcacct gggaattagt ataataacaa tgttnatatt tttgatttac 360  
 attttgtaag gctataattg tatcttttaa gaaaacatac cttggatttc tatgttgaaa 420  
 tggagatttt taagagtttt aaccagctgc tgcagatata ttactcaaaa cagatatagc 480  
 gtataaagat atagtaaagtg catctcctag agtaatatc acttaacaca ttggaaacta 540  
 ttatttttta gatttgaaata tnaatgttat tttttaaaca cttgttatga gttacttggg 600  
 attacatttt gaaatcagtt cattccatga tgcantattc tgggattaga ttaagaaaga 660  
 cggaataa 667

<210> 100  
 <211> 583  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (583)  
 <223> n = A,T,C or G

<400> 100  
 gttttgtttg taagatgatc acagtcattgt tacactgatc taaaggacat atatataacc 60  
 ctttaaaaaa aaaatcactg cctcattctt atttcaagat gaatttctat acagactaga 120  
 tgtttttctg aagatcaatt agacattttg aaaatgattt aaagtgtttt ccttaatgtt 180  
 ctctgaaaac aagtttcttt tgtagtttta accaaaaaag tgcccttttt gtcactggat 240  
 tctcctagca ttcattgattt ttttttcata caatgaaatt aaaattgcta aaatcatgga 300  
 ctggctttct ggttggattt caggttaagat gtgtttaagg ccagagcttt tctcagtatt 360  
 tgattttttt ccccaatatt tgatttttta aaaatataca catnggtgct gcatttatat 420  
 ctgctggttt aaaattctgt catatttcac ttctagcctt ttagttatgg caaatcatat 480  
 ttacttttta cttaaagcat ttggttnattt ggantatctg gttctannct aaaaaaanta 540  
 attctatnaa ttgaantttt ggtactcnnn catatttggg tcc 583

<210> 101  
 <211> 592  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (592)  
 <223> n = A,T,C or G



```

<400> 101
gtggagacgt acaaagagca gccgctcaag acacctggga agaaaaagaa aggcaagccc      60
gggaaacgca aggagcagga aaagaaaaaa cggcgaactc gctctgcctg gttagactct      120
ggagtgactg ggagtgggct agaaggggac cacctgtctg acacctccac aacgtcgctg      180
gagctcgatt cacggaggca ttgaaatddd cagcaganac cttccaagga catattgcag      240
gattctgtaa tagtgaacat atggaaagta ttagaaatat ttattgtctg taaatactgt      300
aaatgcattg gaataaaaact gtctccccc ttgctctatg aaactgcaca ttggtcattg      360
tgaatatttt tttttttgcc aaggctaata caattattat tatcacattt accataattt      420
atdddgtcca ttgatgtatt tattttgtaa atgtatcttg gtgctgctga attdctatat      480
ttttgtaca taatgcnttt anatatacct atcaagtttg ttgataaatg acncaatgaa      540
gtgncncnan ttgngnggtg aatttaatga atgcctaatt ttattatccc aa      592

```

```

<210> 102
<211> 587
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (587)
<223> n = A,T,C or G

```

```

<400> 102
cgctcctaagc acttagacta catcagggaa gaacacagac cacatccctg tcctcatgcg      60
gcttatgttt tctggaagaa agtggagacc nagtccttg ctttagggct ccccggtggt      120
gggctgtgca ntccggtcag ggcgggaagg gaaatgcacc gctgcatgtg aacttacagc      180
ccaggcggat gcccttccc ttagcactac ctggcctcct gcatccctc gcctcatggt      240
cctcccacct tcaanaaatg aanaacccca tgggccccagc cccttgccct gggaaccaa      300
ggcagccttc caaaactcag gggctgaagc anactattag ggcaggggct gactttgggt      360
gacactgccc attccctctc agggcagctc angtcaccn ggnctcttga acccagcctg      420
ttcctttgaa aaagggcaaa actgaaaagg gcttttccta naaaaagaaa aaccagggaa      480
ctttgccagg gcttcnntnt taccaaaacn ncttctcnng gatttttaat tccccattng      540
gcctccactt accnggggcn atgccccaaa attaanaatt tcccatc      587

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```

<210> 103
<211> 496
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (496)
<223> n = A,T,C or G

```

```

<400> 103
anaggactgg ccctacntgc tctctctcgt cctacctatc aatgcccaac atggcagaac      60
ctgcancctt tggncactgc anatggaaac ctctcagtg cttgacatca ccctaccnt      120
gcggtgggtc tccaccacaa ccactttgac tctgtggtcc ctgnanggtg gnttctcctg      180
actggcagga tggaccttan ccnacatata cctctgttcc ctctgctnag anaaagaatt      240
cccttaacat gatataatcc acccatgcaa ntngctactg gccagctac catttaccat      300
ttgcctacag aatttcattc agtctacact ttggcattct ctctggcgat agagtgtggc      360
tgggctgacc gcaaaagggt ccttacacac tggcccccac cctcaaccgt tgacncatca      420
gangcttgcc tctccttct gattnncccc catgttggat atcaggggtg tcnagggatt      480
ggaaaagaaa caaac

```

<210> 104  
 <211> 575  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(575)  
 <223> n = A,T,C or G

<400> 104  
 gcacctgctc tcaatccnnc tctcaccatg atcctccgcc tgcanaaact cctctgccaa 60  
 ctatggangt ggtttcnggg gtggctcttg ccaactggga agaagccgtg gtgtctctac 120  
 ctgttcaact cngtttgtgt ctgggggatc aactnngggc tatggaagcg gctnaactgt 180  
 tgttttggtg gaagggctgg taattggctt tgggaagtng cttatngaag ttggcctnng 240  
 gaagttgcta ttgaaagtng cnttggaagt ngntttggtg gggggttttg ctggtggcct 300  
 ttgttnaatt tgggtgcttt gtnaatggcg gccccctcnc ctgggcaatg aaaaaaatca 360  
 ccnatgcngn aaacctcnac nnaacagcct gggttccct cacctcgaaa aaagttgctc 420  
 ccccccaaa aaaggncaan cccctcaann tggaangttg aaaaaatcct cgaatgggga 480  
 nccnnaaac aaaaancccc cntttcccn gnaanggggg aaataccncc cccccactta 540  
 cnaaaacctt tntaaaaaac cccccgggaa aaaaa 575

<210> 105  
 <211> 619  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(619)  
 <223> n = A,T,C or G

<400> 105  
 cactagtagg atagaaacac tgtgtcccga gagtaaggag agaagctact attgattaga 60  
 gcctaaccac ggttaactgc aagaagaggc gggatacttt cagctttcca tgtaactgta 120  
 tgcataaagc caatgtagtc cagtttctaa gatcatgttc caagctaact gaatcccact 180  
 tcaatacaca ctcatgaact cctgatggaa caataacagg cccaagcctg tggatatgatg 240  
 tgcacacttg ctgactcan aaaaaatact actctcataa atgggtggga gtattttggt 300  
 gacaacctac tttgcttggc tgagtgaagg aatgatattc atatattcat ttattccatg 360  
 gacatttagt tagtgctttt tatataccag gcatgatgct gagtgacact cttgtgtata 420  
 tttccaaatt tttgtacagt cgctgcacat atttgaaatc atatattaag acttccaaaa 480  
 aatgaagtcc ctggtttttc atggcaactt gatcagtaaa ggattcncct ctgtttggtgta 540  
 cttaaaacat ctactatatn gttanatatga aattcctttt cccncctcc cgaaaaaana 600  
 aagtgggtggg gaaaaaaa 619

<210> 106  
 <211> 506  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(506)  
 <223> n = A,T,C or G

<400> 106  
cattggtnct ttcatttgct ntggaagtgt nnatctctaa cagtggacaa agttcccngt 60  
gccttaaact ctgtnacact tttgggaant gaaaanttng tantatgata ggttattctg 120  
angtanagat gttctggata ccattanatn tgcccccngt gtcagaggct catatttgtg 180  
tatgtaaatg gtatntcatt cgctactatn antcaattng aaatanggtc tttgggttat 240  
gaatantnng cagcncanct nanangctgt ctgtngtatt cattgtggtc atagcacctc 300  
acancattgt aacctcnatc nagtgagaca nactagnaanaa ttcctagtga tggctcanga 360  
ttccaaatgg nctcatntcn aatgtttaaa agttanttaa gtgtaagaaa tacagactgg 420  
atgttccacc aactagtacc tgtaatgaacn ggctgtgcc aacacatctc ccttttccat 480  
gactgtggta ncccgcatcg gaaaaa 506

<210> 107  
<211> 452  
<212> DNA  
<213> Homo sapien  
  
<220>  
<221> misc\_feature  
<222> (1)... (452)  
<223> n = A,T,C or G

<400> 107  
gttgagtctg tactaaacag taagatatct caatgaacca taaattcaac tttgtaaaaa 60  
tcttttgaag catagataat attgtttggt aaatgtttct tttgtttggt aaatgtttct 120  
tttaaagacc ctctattct ataaaactct gcatgtagag gcttgtttac ctttctctct 180  
ctaagggtta caataggagt ggtgatttga aaaatataaa attatgagat tggttttcct 240  
gtggcataaa ttgcatcact gtatcatttt cttttttaac cggtaagant ttcagtttgt 300  
tggaaagtaa ctgtganaac ccagtttccc gtccatctcc cttagggact acccatagaa 360  
catgaaaagg tccccacnga agcaagaaga taagtctttc atggctgctg gttgcttaaa 420  
ccactttaaa accaaaaaat tccccttggg aa 452

<210> 108  
<211> 502  
<212> DNA  
<213> Homo sapien  
  
<220>  
<221> misc\_feature  
<222> (1)... (502)  
<223> n = A,T,C or G

<400> 108  
atcttcttcc cttaattagt tnttatttat ntattaaatt ttattgcatg tctggcaaaa 60  
caaaaagaga ttgtagattg gcttctggct ccccaaaagc ccataacaga aagtaccaca 120  
agaccncaac tgaagcttaa aaaatctatc acatgtataa tacctttnga agaacattaa 180  
tanagcatat aaaactttta acatntgctt aatgttgtnc aattataaaa ntaatngaaa 240  
aaaatgtccc tttaacatnc aatatcccac atagtgttat ttnaggggat taccnngnaa 300  
naaaaaaagg gtagaaggga tttaatgaaa actctgcttn ccatttctgt ttanaaacgt 360  
ctccagaaca aaaacttntc aantctttca gctaaccgca tttgagctna ggccactcaa 420  
aaactccatt agnccactt tctaanggtc tctanagctt actaancctt ttgaccctt 480  
accctggnta ctctgcccct ca 502

<210> 109  
<211> 1308

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 109

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acccgaggtc tcgctaaaat catcatggat tcacttggcg ccgtcagcac tcgacttggg      60
tttgatcttt tcaaagagct gaagaaaaca aatgatggca acatcttctt ttcccctgtg      120
ggcatcttga ctgcaattgg catggtcctc ctggggaccc gaggagccac cgcttcccag      180
ttggaggagg tgtttcactc tgaaaaagag acgaagagct caagaataaa ggctgaagaa      240
aaagaggtga ttgagaacac agaagcagta catcaacaat tccaaaagtt tttgactgaa      300
ataagcaaac tcactaatga ttatgaactg aacataacca acaggctgtt tggagaaaaa      360
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&lt;210&gt; 110

&lt;211&gt; 391

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 110

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Met Asp Ser Leu Gly Ala Val Ser Thr Arg Leu Gly Phe Asp Leu Phe
 1          5          10          15
Lys Glu Leu Lys Thr Asn Asp Gly Asn Ile Phe Phe Ser Pro Val
 20          25          30
Gly Ile Leu Thr Ala Ile Gly Met Val Leu Leu Gly Thr Arg Gly Ala
 35          40          45
Thr Ala Ser Gln Leu Glu Glu Val Phe His Ser Glu Lys Glu Thr Lys
 50          55          60
Ser Ser Arg Ile Lys Ala Glu Glu Lys Glu Val Ile Glu Asn Thr Glu
 65          70          75          80
Ala Val His Gln Gln Phe Gln Lys Phe Leu Thr Glu Ile Ser Lys Leu
 85          90          95
Thr Asn Asp Tyr Glu Leu Asn Ile Thr Asn Arg Leu Phe Gly Glu Lys
100          105          110
Thr Tyr Leu Phe Leu Gln Lys Tyr Leu Asp Tyr Val Glu Lys Tyr Tyr
115          120          125
His Ala Ser Leu Glu Pro Val Asp Phe Val Asn Ala Ala Asp Glu Ser
130          135          140
Arg Lys Lys Ile Asn Ser Trp Val Glu Ser Lys Thr Asn Glu Lys Ile
145          150          155          160
Lys Asp Leu Phe Pro Asp Gly Ser Ile Ser Ser Ser Thr Lys Leu Val
165          170          175

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Leu Val Asn Met Val Tyr Phe Lys Gly Gln Trp Asp Arg Glu Phe Lys  
 180 185 190  
 Lys Glu Asn Thr Lys Glu Glu Lys Phe Trp Met Asn Lys Ser Thr Ser  
 195 200 205  
 Lys Ser Val Gln Met Met Thr Gln Ser His Ser Phe Ser Phe Thr Phe  
 210 215 220  
 Leu Glu Asp Leu Gln Ala Lys Ile Leu Gly Ile Pro Tyr Lys Asn Asn  
 225 230 235 240  
 Asp Leu Ser Met Phe Val Leu Leu Pro Asn Asp Ile Asp Gly Leu Glu  
 245 250 255  
 Lys Ile Ile Asp Lys Ile Ser Pro Glu Lys Leu Val Glu Trp Thr Ser  
 260 265 270  
 Pro Gly His Met Glu Glu Arg Lys Val Asn Leu His Leu Pro Arg Phe  
 275 280 285  
 Glu Val Glu Asp Ser Tyr Asp Leu Glu Ala Val Leu Ala Ala Met Gly  
 290 295 300  
 Met Gly Asp Ala Phe Ser Glu His Lys Ala Asp Tyr Ser Gly Met Ser  
 305 310 315 320  
 Ser Gly Ser Gly Leu Tyr Ala Gln Lys Phe Leu His Ser Ser Phe Val  
 325 330 335  
 Ala Val Thr Glu Glu Gly Thr Glu Ala Ala Ala Thr Gly Ile Gly  
 340 345 350  
 Phe Thr Val Thr Ser Ala Pro Gly His Glu Asn Val His Cys Asn His  
 355 360 365  
 Pro Phe Leu Phe Phe Ile Arg His Asn Glu Ser Asn Ser Ile Leu Phe  
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 Phe Gly Arg Phe Ser Ser Pro  
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&lt;210&gt; 111

&lt;211&gt; 1419

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 111

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<210> 112
<211> 400
<212> PRT
<213> Homo sapien

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<400> 112
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Lys Glu Leu Lys Lys Thr Asn Asp Gly Asn Ile Phe Phe Ser Pro Val
      20          25          30
Gly Ile Leu Thr Ala Ile Gly Met Val Leu Leu Gly Thr Arg Gly Ala
      35          40          45
Thr Ala Ser Gln Leu Glu Glu Val Phe His Ser Glu Lys Glu Thr Lys
      50          55          60
Ser Ser Arg Ile Lys Ala Glu Glu Lys Glu Val Val Arg Ile Lys Ala
      65          70          75          80
Glu Gly Lys Glu Ile Glu Asn Thr Glu Ala Val His Gln Gln Phe Gln
      85          90          95
Lys Phe Leu Thr Glu Ile Ser Lys Leu Thr Asn Asp Tyr Glu Leu Asn
      100          105          110
Ile Thr Asn Arg Leu Phe Gly Glu Lys Thr Tyr Leu Phe Leu Gln Lys
      115          120          125
Tyr Leu Asp Tyr Val Glu Lys Tyr Tyr His Ala Ser Leu Glu Pro Val
      130          135          140
Asp Phe Val Asn Ala Ala Asp Glu Ser Arg Lys Lys Ile Asn Ser Trp
      145          150          155          160
Val Glu Ser Lys Thr Asn Glu Lys Ile Lys Asp Leu Phe Pro Asp Gly
      165          170          175
Ser Ile Ser Ser Ser Thr Lys Leu Val Leu Val Asn Met Val Tyr Phe
      180          185          190
Lys Gly Gln Trp Asp Arg Glu Phe Lys Lys Glu Asn Thr Lys Glu Glu
      195          200          205
Lys Phe Trp Met Asn Lys Ser Thr Ser Lys Ser Val Gln Met Met Thr
      210          215          220
Gln Ser His Ser Phe Ser Phe Thr Phe Leu Glu Asp Leu Gln Ala Lys
      225          230          235          240
Ile Leu Gly Ile Pro Tyr Lys Asn Asn Asp Leu Ser Met Phe Val Leu
      245          250          255
Leu Pro Asn Asp Ile Asp Gly Leu Glu Lys Ile Ile Asp Lys Ile Ser
      260          265          270
Pro Glu Lys Leu Val Glu Trp Thr Ser Pro Gly His Met Glu Glu Arg
      275          280          285
Lys Val Asn Leu His Leu Pro Arg Phe Glu Val Glu Asp Ser Tyr Asp
      290          295          300
Leu Glu Ala Val Leu Ala Ala Met Gly Met Gly Asp Ala Phe Ser Glu
      305          310          315          320
His Lys Ala Asp Tyr Ser Gly Met Ser Ser Gly Ser Gly Leu Tyr Ala
      325          330          335
Gln Lys Phe Leu His Ser Ser Phe Val Ala Val Thr Glu Glu Gly Thr
      340          345          350

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Glu Ala Ala Ala Ala Thr Gly Ile Gly Phe Thr Val Thr Ser Ala Pro  
 355 360 365  
 Gly His Glu Asn Val His Cys Asn His Pro Phe Leu Phe Phe Ile Arg  
 370 375 380  
 His Asn Glu Ser Asn Ser Ile Leu Phe Phe Gly Arg Phe Ser Ser Pro  
 385 390 395 400

<210> 113  
 <211> 957  
 <212> DNA  
 <213> Homo sapien

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<210> 114  
 <211> 161  
 <212> PRT  
 <213> Homo sapien

<400> 114  
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 20 25 30  
 Phe Val Pro Thr Thr Lys Glu Pro Cys His Ser Lys Val Pro Gln Pro  
 35 40 45  
 Gly Asn Thr Lys Ile Pro Glu Pro Gly Cys Thr Lys Val Pro Glu Pro  
 50 55 60  
 Gly Cys Thr Lys Val Pro Glu Pro Gly Cys Thr Lys Val Pro Glu Pro  
 65 70 75 80  
 Gly Cys Thr Lys Val Pro Glu Pro Gly Cys Thr Lys Val Pro Glu Pro  
 85 90 95  
 Gly Tyr Thr Lys Val Pro Glu Pro Gly Ser Ile Lys Val Pro Asp Gln  
 100 105 110  
 Gly Phe Ile Lys Phe Pro Glu Pro Gly Ala Ile Lys Val Pro Glu Gln  
 115 120 125  
 Gly Tyr Thr Lys Val Pro Val Pro Gly Tyr Thr Lys Val Pro Glu Pro  
 130 135 140  
 Cys Pro Ser Thr Val Thr Pro Gly Pro Ala Gln Gln Lys Thr Lys Gln

145  
Lys

150

155

160

<210> 115  
<211> 506  
<212> DNA  
<213> Homo sapien  
  
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<221> misc\_feature  
<222> (1)...(506)  
<223> n = A,T,C or G

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<210> 116  
<211> 3079  
<212> DNA  
<213> Homo sapien

<400> 116  
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&lt;210&gt; 117

&lt;211&gt; 6921

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 117

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8948

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 <211> 587  
 <212> DNA  
 <213> Homo sapien  
  
 <220>  
 <221> misc\_feature  
 <222> (1)...(587)  
 <223> n = A,T,C or G

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<210> 121  
 <211> 619  
 <212> DNA  
 <213> Homo sapien  
  
 <220>  
 <221> misc\_feature  
 <222> (1)...(619)  
 <223> n = A,T,C or G

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 aagtgggtggg gaaaaaaaaa 619

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 <211> 1475  
 <212> DNA  
 <213> Homo sapien

<400> 122  
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&lt;210&gt; 123

&lt;211&gt; 2294

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 123

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&lt;210&gt; 124

&lt;211&gt; 956

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 124

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&lt;210&gt; 125

&lt;211&gt; 486

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(486)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 125

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 <212> DNA  
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&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 127

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&lt;210&gt; 128

&lt;211&gt; 374

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 128

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&lt;211&gt; 546

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

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<211> 5156

<212> DNA

<213> Homo sapien

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&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 131

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&lt;211&gt; 590

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 132

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&lt;210&gt; 133

&lt;211&gt; 581

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 133

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&lt;210&gt; 134

&lt;211&gt; 4797

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

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&lt;223&gt; n = A, T, C or G

&lt;400&gt; 134

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&lt;211&gt; 2856

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 135

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&lt;210&gt; 136

&lt;211&gt; 356

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 136

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&lt;210&gt; 137

&lt;211&gt; 356

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (356)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 137

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&lt;210&gt; 138

&lt;211&gt; 353

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 138

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&lt;210&gt; 139

&lt;211&gt; 371

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 139

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&lt;210&gt; 140

&lt;211&gt; 370

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 140

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&lt;210&gt; 141

&lt;211&gt; 371

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 141

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&lt;210&gt; 142

&lt;211&gt; 343

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 142

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&lt;210&gt; 143

&lt;211&gt; 354

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 143

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&lt;210&gt; 144

&lt;211&gt; 353

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 144

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&lt;210&gt; 145

&lt;211&gt; 371

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 145

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 <211> 620  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(620)  
 <223> n = A,T,C or G

<400> 149

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&lt;210&gt; 150

&lt;211&gt; 371

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 150

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&lt;210&gt; 151

&lt;211&gt; 4655

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 151

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<210> 152  
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 <212> PRT  
 <213> Homo sapien

<400> 152  
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 Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser  
 35 40 45  
 Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala  
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 Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro  
 65 70 75 80  
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 Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala  
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 Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly  
 115 120 125  
 Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr  
 130 135 140  
 Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn  
 145 150 155 160  
 Glu Gly Gln Ile Ala Pro Ser Ser His Leu Ile Arg Val Glu Gly Asn  
 165 170 175  
 Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val  
 180 185 190  
 Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val  
 195 200 205  
 Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg  
 210 215 220  
 Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val  
 225 230 235 240  
 Leu Gly Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg  
 245 250 255  
 Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp  
 260 265 270  
 Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr  
 275 280 285  
 His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp  
 290 295 300  
 Glu Leu Val Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu  
 305 310 315 320  
 Val Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Leu Gln His  
 325 330 335  
 Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln Gln His Gln His Leu  
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 355 360 365  
 Ser Pro Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val  
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Ile	Pro	Asp	Gly	Met	Gly	Ala	Asn	Ile	Pro	Met	Met	Gly	Thr	His	Met
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Pro	Met	Ala	Gly	Asp	Met	Asn	Gly	Leu	Ser	Pro	Thr	Gln	Ala	Leu	Pro
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Pro	Pro	Leu	Ser	Met	Pro	Ser	Thr	Ser	His	Cys	Thr	Pro	Pro	Pro	Pro
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Tyr	Pro	Thr	Asp	Cys	Ser	Ile	Val	Ser	Phe	Leu	Ala	Arg	Leu	Gly	Cys
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Gln	Ile	Glu	His	Tyr	Ser	Met	Asp	Asp	Leu	Ala	Ser	Leu	Lys	Ile	Pro
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Ala	Ser	Thr	Val	Ser	Val	Gly	Ser	Ser	Glu	Thr	Arg	Gly	Glu	Arg	Val
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Arg	Asp	Glu	Trp	Asn	Asp	Phe	Asn	Phe	Asp	Met	Asp	Ala	Arg	Arg	Asn
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&lt;210&gt; 153

&lt;211&gt; 2007

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 153

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&lt;210&gt; 154

&lt;211&gt; 2148

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 154

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 <212> PRT  
 <213> Homo sapien

<400> 155  
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 35 40 45  
 Ala Ala Val Ser Ser Ile Phe Asn Ser Pro Glu Glu Phe Leu Gly Lys  
 50 55 60  
 Ala Val Gly Leu Ser Ala Glu Ala Leu Thr Ile Gln Gln Tyr Ala Asp  
 65 70 75 80  
 Val Leu Ser Lys Ala Leu Gly Lys Glu Val Arg Asp Ala Lys Ile Thr  
 85 90 95  
 Pro Glu Ala Phe Glu Lys Leu Gly Phe Pro Ala Ala Lys Glu Ile Ala  
 100 105 110  
 Asn Met Cys Arg Phe Tyr Glu Met Lys Pro Asp Arg Asp Val Asn Leu  
 115 120 125  
 Thr His Gln Leu Asn Pro Lys Val Lys Ser Phe Ser Gln Phe Ile Ser  
 130 135 140  
 Glu Asn Gln Gly Ala Phe Lys Gly Met  
 145 150

<210> 156  
 <211> 128  
 <212> PRT  
 <213> Homo sapien

<400> 156  
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 Trp Arg Pro Val Lys Ala Ser Asp Gly Asp Tyr Tyr Thr Leu Ala Val  
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 Pro Met Gly Asp Val Pro Met Asp Gly Ile Ser Val Ala Asp Ile Gly  
 35 40 45  
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 Val Leu Ser Lys Ala Leu Gly Lys Glu Val Arg Asp Ala Lys Thr Ile  
 85 90 95  
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 <211> 424  
 <212> DNA  
 <213> Homo sapien

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&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(424)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 157

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&lt;210&gt; 158

&lt;211&gt; 2099

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 158

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<212> PRT  
<213> Homo sapien

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Tyr Tyr Arg His Glu Thr Thr Arg Lys Phe Arg Arg Gly Glu Lys Arg  
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<211> 3951  
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&lt;210&gt; 161

&lt;211&gt; 943

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 161

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Ile Thr Glu Ala Ser Phe Tyr Leu Phe Asn Ala Thr Lys Arg Arg Val
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Phe Phe Arg Asn Ile Lys Ile Leu Ile Pro Ala Thr Trp Lys Ala Asn
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Val Thr Asp Trp Tyr Gly Ala His Gly Asp Asp Pro Tyr Thr Leu Gln
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Tyr Arg Gly Cys Gly Lys Glu Gly Lys Tyr Ile His Phe Thr Pro Asn
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Val Phe Val His Glu Trp Ala His Leu Arg Trp Gly Val Phe Asp Glu
165    170    175
Tyr Asn Asn Asp Lys Pro Phe Tyr Ile Asn Gly Gln Asn Gln Ile Lys
180    185    190
Val Thr Arg Cys Ser Ser Asp Ile Thr Gly Ile Phe Val Cys Glu Lys
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Gly Pro Cys Pro Gln Glu Asn Cys Ile Ile Ser Lys Leu Phe Lys Glu
210    215    220
Gly Cys Thr Phe Ile Tyr Asn Ser Thr Gln Asn Ala Thr Ala Ser Ile
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Thr His Asn Gln Glu Ala Pro Asn Leu Gln Asn Gln Met Cys Ser Leu
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Phe Pro Met Asn Gly Thr Glu Leu Pro Pro Pro Pro Thr Phe Ser Leu
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 340 345 350  
 Ser Phe Asp Ser Lys Gly Glu Ile Arg Ala Gln Leu His Gln Ile Asn  
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 Ser Asn Asp Asp Arg Lys Leu Val Ser Tyr Leu Pro Thr Thr Val  
 370 375 380  
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 405 410 415  
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 435 440 445  
 Ala Ala Pro Asn Leu Glu Glu Leu Ser Arg Leu Thr Gly Gly Leu Lys  
 450 455 460  
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 515 520 525  
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 Gly Arg Lys Tyr Tyr Thr Asn Asn Phe Ile Thr Asn Leu Thr Phe Arg  
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 Thr Ala Ser Leu Trp Ile Pro Gly Thr Ala Lys Pro Gly His Trp Thr  
 565 570 575  
 Tyr Thr Leu Asn Asn Thr His His Ser Leu Gln Ala Leu Lys Val Thr  
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 Val Thr Ser Arg Ala Ser Asn Ser Ala Val Pro Pro Ala Thr Val Glu  
 595 600 605  
 Ala Phe Val Glu Arg Asp Ser Leu His Phe Pro His Pro Val Met Ile  
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 Thr Ala Thr Val Glu Pro Glu Thr Gly Asp Pro Val Thr Leu Arg Leu  
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 Arg Lys Trp Gly Phe Ser Arg Val Ser Ser Gly Gly Ser Phe Ser Val

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tgtatcttgg	tgctgctgaa	tttctatatt	ttttgtaaca	taatgcactt	tagatataca	960
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aatgcctaaa	tataattatc	caaattgatt	ttcctttgtg	catgtaaaaa	taacagtatt	1080
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&lt;210&gt; 164

&lt;211&gt; 1310

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 164

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gagacgtgta	aacacactac	ttatcattga	tgcataata	aaaccatttt	attttcgcta	180
ttatttcaga	ggaagcgcct	ctgatttgtt	tcttttttcc	ctttttgctc	tttctggctg	240
tgtggtttgg	agaaagcaca	gttggagtag	ccggttgcta	aataagtccc	gagcgcgagc	300
ggagacgatg	cagcggagac	tggttcagca	gtggagcgtc	gcggtgttcc	tgctgagcta	360
cgcggtgccc	tcctgcgggc	gctcgggtga	gggtctcagc	cgccgcctca	aaagagctgt	420
gtctgaacat	cagctcctcc	atgacaaggg	gaagtccatc	caagatttac	ggcgacgatt	480
cttccttcac	catctgatcg	cagaaatcca	cacagctgaa	atcagagcta	cctcggaggt	540
gtcccctaac	tccaagccct	ctcccaacac	aaagaaccac	cccgtccgat	ttgggtctga	600
tgatgagggc	agatacctaa	ctcaggaaac	taacaagggt	gagacgtaca	aagagcagcc	660
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&lt;210&gt; 165

&lt;211&gt; 177

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 165

Met	Gln	Arg	Arg	Leu	Val	Gln	Gln	Trp	Ser	Val	Ala	Val	Phe	Leu	Leu
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Ser	Tyr	Ala	Val	Pro	Ser	Cys	Gly	Arg	Ser	Val	Glu	Gly	Leu	Ser	Arg
				20				25						30	
Arg	Leu	Lys	Arg	Ala	Val	Ser	Glu	His	Gln	Leu	Leu	His	Asp	Lys	Gly
				35				40						45	
Lys	Ser	Ile	Gln	Asp	Leu	Arg	Arg	Arg	Phe	Phe	Leu	His	His	Leu	Ile

50		55		60											
Ala	Glu	Ile	His	Thr	Ala	Glu	Ile	Arg	Ala	Thr	Ser	Glu	Val	Ser	Pro
65					70					75					80
Asn	Ser	Lys	Pro	Ser	Pro	Asn	Thr	Lys	Asn	His	Pro	Val	Arg	Phe	Gly
			85						90					95	
Ser	Asp	Asp	Glu	Gly	Arg	Tyr	Leu	Thr	Gln	Glu	Thr	Asn	Lys	Val	Glu
		100						105					110		
Thr	Tyr	Lys	Glu	Gln	Pro	Leu	Lys	Thr	Pro	Gly	Lys	Lys	Lys	Lys	Gly
	115						120						125		
Lys	Pro	Gly	Lys	Arg	Lys	Glu	Gln	Glu	Lys	Lys	Lys	Arg	Arg	Thr	Arg
	130					135					140				
Ser	Ala	Trp	Leu	Asp	Ser	Gly	Val	Thr	Gly	Ser	Gly	Leu	Glu	Gly	Asp
145					150					155					160
His	Leu	Ser	Asp	Thr	Ser	Thr	Thr	Ser	Leu	Glu	Leu	Asp	Ser	Arg	Arg
			165						170					175	

His

<210> 166  
 <211> 177  
 <212> PRT  
 <213> Homo sapien

<400> 166

Met	Gln	Arg	Arg	Leu	Val	Gln	Gln	Trp	Ser	Val	Ala	Val	Phe	Leu	Leu
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Ser	Tyr	Ala	Val	Pro	Ser	Cys	Gly	Arg	Ser	Val	Glu	Gly	Leu	Ser	Arg
		20						25					30		
Arg	Leu	Lys	Arg	Ala	Val	Ser	Glu	His	Gln	Leu	Leu	His	Asp	Lys	Gly
	35						40					45			
Lys	Ser	Ile	Gln	Asp	Leu	Arg	Arg	Arg	Phe	Phe	Leu	His	His	Leu	Ile
	50					55				60					
Ala	Glu	Ile	His	Thr	Ala	Glu	Ile	Arg	Ala	Thr	Ser	Glu	Val	Ser	Pro
65					70					75					80
Asn	Ser	Lys	Pro	Ser	Pro	Asn	Thr	Lys	Asn	His	Pro	Val	Arg	Phe	Gly
			85						90					95	
Ser	Asp	Asp	Glu	Gly	Arg	Tyr	Leu	Thr	Gln	Glu	Thr	Asn	Lys	Val	Glu
		100						105					110		
Thr	Tyr	Lys	Glu	Gln	Pro	Leu	Lys	Thr	Pro	Gly	Lys	Lys	Lys	Lys	Gly
	115						120						125		
Lys	Pro	Gly	Lys	Arg	Lys	Glu	Gln	Glu	Lys	Lys	Lys	Arg	Arg	Thr	Arg
	130					135				140					
Ser	Ala	Trp	Leu	Asp	Ser	Gly	Val	Thr	Gly	Ser	Gly	Leu	Glu	Gly	Asp
145					150					155					160
His	Leu	Ser	Asp	Thr	Ser	Thr	Thr	Ser	Leu	Glu	Leu	Asp	Ser	Arg	Arg
			165						170					175	

His

<210> 167  
 <211> 3362  
 <212> DNA  
 <213> Homo sapien

<400> 167

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ttcagaactc	ccattcctgg	gagctggagt	acagcttcaa	gacaatgggt	ataatggatt	180
gctcattgca	attaatcctc	aggtacctga	gaatcagaac	ctcatctcaa	acattaagga	240
aatgataact	gaagcttcat	tttacctatt	taatgctacc	aagagaagag	tattttttcag	300
aaatataaag	attttaatac	ctgccacatg	gaaagctaata	aataacagca	aaataaaaaca	360
agaatcatat	gaaaaggcaa	atgtcatagt	gactgactgg	tatggggcac	atggagatga	420
tccatacacc	ctacaataca	gaggggtgtg	aaaagaggga	aaatacattc	atttcacacc	480
taatttccta	ctgaatgata	acttaacagc	tggctacgga	tcacgaggcc	gagtgtttgt	540
ccatgaatgg	gccacacctc	gttgggggtg	gttcgatgag	tataacaatg	acaaaccttt	600
ctacataaat	gggcaaaatc	aaattaaagt	gacaagggtg	tcactctgaca	tcacaggcat	660
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agaaggatgc	accttttatct	acaatagcac	ccaaaatgca	actgcatcaa	taatgttcat	780
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aaacctacag	aaccagatgt	gcagcctcag	aagtgcattg	gatgtaatca	cagactctgc	900
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 tt 3362

<210> 168  
 <211> 2784  
 <212> DNA  
 <213> Homo sapien

<400> 168

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taataataac	agcaaaataa	aacaagaatc	atatgaaaag	gcaaatgtca	tagtgactga	420
ctggtatggg	gcacatggag	atgatccata	caccctacaa	tacagagggg	gtggaaaaga	480
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ctgccagaga ttatcttata ttga

2784

&lt;210&gt; 169

&lt;211&gt; 592

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 169

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 Thr Leu Leu Val Ala Leu Ser Ser Glu Leu Pro Phe Leu Gly Ala Gly  
 20 25 30  
 Val Gln Leu Gln Asp Asn Gly Tyr Asn Gly Leu Leu Ile Ala Ile Asn  
 35 40 45  
 Pro Gln Val Pro Glu Asn Gln Asn Leu Ile Ser Asn Ile Lys Glu Met  
 50 55 60  
 Ile Thr Glu Ala Ser Phe Tyr Leu Phe Asn Ala Thr Lys Arg Arg Val  
 65 70 75 80  
 Phe Phe Arg Asn Ile Lys Ile Leu Ile Pro Ala Thr Trp Lys Ala Asn  
 85 90 95  
 Asn Asn Ser Lys Ile Lys Gln Glu Ser Tyr Glu Lys Ala Asn Val Ile  
 100 105 110  
 Val Thr Asp Trp Tyr Gly Ala His Gly Asp Asp Pro Tyr Thr Leu Gln  
 115 120 125  
 Tyr Arg Gly Cys Gly Lys Glu Gly Lys Tyr Ile His Phe Thr Pro Asn  
 130 135 140  
 Phe Leu Leu Asn Asp Asn Leu Thr Ala Gly Tyr Gly Ser Arg Gly Arg  
 145 150 155 160  
 Val Phe Val His Glu Trp Ala His Leu Arg Trp Gly Val Phe Asp Glu  
 165 170 175  
 Tyr Asn Asn Asp Lys Pro Phe Tyr Ile Asn Gly Gln Asn Gln Ile Lys  
 180 185 190  
 Val Thr Arg Cys Ser Ser Asp Ile Thr Gly Ile Phe Val Cys Glu Lys  
 195 200 205  
 Gly Pro Cys Pro Gln Glu Asn Cys Ile Ile Ser Lys Leu Phe Lys Glu  
 210 215 220  
 Gly Cys Thr Phe Ile Tyr Asn Ser Thr Gln Asn Ala Thr Ala Ser Ile  
 225 230 235 240  
 Met Phe Met Gln Ser Leu Ser Ser Val Val Glu Phe Cys Asn Ala Ser  
 245 250 255  
 Thr His Asn Gln Glu Ala Pro Asn Leu Gln Asn Gln Met Cys Ser Leu  
 260 265 270  
 Arg Ser Ala Trp Asp Val Ile Thr Asp Ser Ala Asp Phe His His Ser  
 275 280 285  
 Phe Pro Met Asn Gly Thr Glu Leu Pro Pro Pro Pro Thr Phe Ser Leu  
 290 295 300  
 Val Glu Ala Gly Asp Lys Val Val Cys Leu Val Leu Asp Val Ser Ser  
 305 310 315 320  
 Lys Met Ala Glu Ala Asp Arg Leu Leu Gln Leu Gln Gln Ala Ala Glu  
 325 330 335  
 Phe Tyr Leu Met Gln Ile Val Glu Ile His Thr Phe Val Gly Ile Ala  
 340 345 350  
 Ser Phe Asp Ser Lys Gly Glu Ile Arg Ala Gln Leu His Gln Ile Asn  
 355 360 365  
 Ser Asn Asp Asp Arg Lys Leu Leu Val Ser Tyr Leu Pro Thr Thr Val

370		375		380											
Ser	Ala	Lys	Thr	Asp	Ile	Ser	Ile	Cys	Ser	Gly	Leu	Lys	Lys	Gly	Phe
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Glu	Val	Val	Glu	Lys	Leu	Asn	Gly	Lys	Ala	Tyr	Gly	Ser	Val	Met	Ile
				405					410					415	
Leu	Val	Thr	Ser	Gly	Asp	Asp	Lys	Leu	Leu	Gly	Asn	Cys	Leu	Pro	Thr
			420					425					430		
Val	Leu	Ser	Ser	Gly	Ser	Thr	Ile	His	Ser	Ile	Ala	Leu	Gly	Ser	Ser
		435				440					445				
Ala	Ala	Pro	Asn	Leu	Glu	Glu	Leu	Ser	Arg	Leu	Thr	Gly	Gly	Leu	Lys
450					455					460					
Phe	Phe	Val	Pro	Asp	Ile	Ser	Asn	Ser	Asn	Ser	Met	Ile	Asp	Ala	Phe
465				470						475					480
Ser	Arg	Ile	Ser	Ser	Gly	Thr	Gly	Asp	Ile	Phe	Gln	Gln	His	Ile	Gln
			485					490						495	
Leu	Glu	Ser	Thr	Gly	Glu	Asn	Val	Lys	Pro	His	His	Gln	Leu	Lys	Asn
		500					505						510		
Thr	Val	Thr	Val	Asp	Asn	Thr	Val	Gly	Asn	Asp	Thr	Met	Phe	Leu	Val
	515					520					525				
Thr	Trp	Gln	Ala	Ser	Gly	Pro	Pro	Glu	Ile	Ile	Leu	Phe	Asp	Pro	Asp
530					535					540					
Gly	Arg	Lys	Tyr	Tyr	Thr	Asn	Asn	Phe	Ile	Thr	Asn	Leu	Thr	Phe	Arg
545				550					555					560	
Thr	Ala	Ser	Leu	Trp	Ile	Pro	Gly	Thr	Ala	Lys	Pro	Gly	His	Trp	Thr
			565					570					575		
Tyr	Thr	Leu	Met	Cys	Phe	His	His	Ala	Lys	Leu	Leu	Thr	Trp	Lys	Leu
		580					585					590			

&lt;210&gt; 170

&lt;211&gt; 791

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 170

Met	Thr	Gln	Arg	Ser	Ile	Ala	Gly	Pro	Ile	Cys	Asn	Leu	Lys	Phe	Val
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Phe	Phe	Arg	Asn	Ile	Lys	Ile	Leu	Ile	Pro	Ala	Thr	Trp	Lys	Ala	Asn
		85					90					95			
Asn	Asn	Ser	Lys	Ile	Lys	Gln	Glu	Ser	Tyr	Glu	Lys	Ala	Asn	Val	Ile
	100					105				110					
Val	Thr	Asp	Trp	Tyr	Gly	Ala	His	Gly	Asp	Asp	Pro	Tyr	Thr	Leu	Gln
	115				120				125						
Tyr	Arg	Gly	Cys	Gly	Lys	Glu	Gly	Lys	Tyr	Ile	His	Phe	Thr	Pro	Asn
130				135					140						
Phe	Leu	Leu	Asn	Asp	Asn	Leu	Thr	Ala	Gly	Tyr	Gly	Ser	Arg	Gly	Arg
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Val	Phe	Val	His	Glu	Trp	Ala	His	Leu	Arg	Trp	Gly	Val	Phe	Asp	Glu

				165					170					175		
Tyr	Asn	Asn	Asp	Lys	Pro	Phe	Tyr	Ile	Asn	Gly	Gln	Asn	Gln	Ile	Lys	
			180					185					190			
Val	Thr	Arg	Cys	Ser	Ser	Asp	Ile	Thr	Gly	Ile	Phe	Val	Cys	Glu	Lys	
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225					230					235					240	
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			245					250						255		
Thr	His	Asn	Gln	Glu	Ala	Pro	Asn	Leu	Gln	Asn	Gln	Met	Cys	Ser	Leu	
			260					265					270			
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Val	Glu	Ala	Gly	Asp	Lys	Val	Val	Cys	Leu	Val	Leu	Asp	Val	Ser	Ser	
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Lys	Met	Ala	Glu	Ala	Asp	Arg	Leu	Leu	Gln	Leu	Gln	Gln	Ala	Ala	Glu	
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Phe	Tyr	Leu	Met	Gln	Ile	Val	Glu	Ile	His	Thr	Phe	Val	Gly	Ile	Ala	
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			405						410					415		
Leu	Val	Thr	Ser	Gly	Asp	Asp	Lys	Leu	Leu	Gly	Asn	Cys	Leu	Pro	Thr	
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Val	Leu	Ser	Ser	Gly	Ser	Thr	Ile	His	Ser	Ile	Ala	Leu	Gly	Ser	Ser	
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Ala	Ala	Pro	Asn	Leu	Glu	Glu	Leu	Ser	Arg	Leu	Thr	Gly	Gly	Leu	Lys	
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Phe	Phe	Val	Pro	Asp	Ile	Ser	Asn	Ser	Asn	Ser	Met	Ile	Asp	Ala	Phe	
465					470					475					480	
Ser	Arg	Ile	Ser	Ser	Gly	Thr	Gly	Asp	Ile	Phe	Gln	Gln	His	Ile	Gln	
			485						490					495		
Leu	Glu	Ser	Thr	Gly	Glu	Asn	Val	Lys	Pro	His	His	Gln	Leu	Lys	Asn	
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Thr	Val	Thr	Val	Asp	Asn	Thr	Val	Gly	Asn	Asp	Thr	Met	Phe	Leu	Val	
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Ala	Phe	Val	Glu	Arg	Asp	Ser	Leu	His	Phe	Pro	His	Pro	Val	Met	Ile
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Tyr	Ala	Asn	Val	Lys	Gln	Gly	Phe	Tyr	Pro	Ile	Leu	Asn	Ala	Thr	Val
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Thr	Ala	Thr	Val	Glu	Pro	Glu	Thr	Gly	Asp	Pro	Val	Thr	Leu	Arg	Leu
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Leu	Asp	Asp	Gly	Ala	Gly	Ala	Asp	Val	Ile	Lys	Asn	Asp	Gly	Ile	Tyr
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Ser	Arg	Tyr	Phe	Phe	Ser	Phe	Ala	Asn	Gly	Arg	Tyr	Ser	Leu	Lys	
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Val	His	Val	Asn	His	Ser	Pro	Ser	Ile	Ser	Thr	Pro	Ala	His	Ser	Ile
		690				695					700				
Pro	Gly	Ser	His	Ala	Met	Tyr	Val	Pro	Gly	Tyr	Thr	Ala	Asn	Gly	Asn
705					710					715					720
Ile	Gln	Met	Asn	Ala	Pro	Arg	Lys	Ser	Val	Gly	Arg	Asn	Glu	Glu	Glu
				725						730				735	
Arg	Lys	Trp	Gly	Phe	Ser	Arg	Val	Ser	Ser	Gly	Gly	Ser	Phe	Ser	Val
			740					745					750		
Leu	Gly	Val	Pro	Ala	Gly	Pro	His	Pro	Asp	Val	Phe	Pro	Pro	Cys	Lys
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Ile	Ile	Asp	Leu	Glu	Ala	Val	Asn	Arg	Arg	Gly	Ile	Asp	Pro	Ile	Leu
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Asp	Ser	Thr	Trp	Arg	Arg	Leu									
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&lt;210&gt; 171

&lt;211&gt; 1491

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 171

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1491

<210> 172

<211> 364

<212> PRT

<213> Homo sapien

<400> 172

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			20					25					30		
Asn	Thr	Gln	Arg	Lys	Lys	Ser	Gln	Glu	Lys	Met	Arg	Glu	Val	Thr	Asp
			35				40					45			
Ser	Pro	Gly	Arg	Pro	Arg	Glu	Leu	Thr	Ile	Pro	Gln	Thr	Ser	Ser	His
	50					55					60				
Gly	Ala	Asn	Arg	Phe	Val	Pro	Lys	Ser	Lys	Ala	Leu	Glu	Ala	Val	Lys
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Leu	Ala	Ile	Glu	Ala	Gly	Phe	His	His	Ile	Asp	Ser	Ala	His	Val	Tyr
				85					90					95	
Asn	Asn	Glu	Glu	Gln	Val	Gly	Leu	Ala	Ile	Arg	Ser	Lys	Ile	Ala	Asp
			100					105					110		
Gly	Ser	Val	Lys	Arg	Glu	Asp	Ile	Phe	Tyr	Thr	Ser	Lys	Leu	Trp	Ser
		115					120					125			
Asn	Ser	His	Arg	Pro	Glu	Leu	Val	Arg	Pro	Ala	Leu	Glu	Arg	Ser	Leu
	130					135					140				
Lys	Asn	Leu	Gln	Leu	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Ile	His	Phe	Pro
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Val	Ser	Val	Lys	Pro	Gly	Glu	Glu	Val	Ile	Pro	Lys	Asp	Glu	Asn	Gly
				165					170					175	
Lys	Ile	Leu	Phe	Asp	Thr	Val	Asp	Leu	Cys	Ala	Thr	Trp	Glu	Ala	Met
			180					185					190		
Glu	Lys	Cys	Lys	Asp	Ala	Gly	Leu	Ala	Lys	Ser	Ile	Gly	Val	Ser	Asn
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Tyr	Lys	Pro	Val	Cys	Asn	Gln	Val	Glu	Cys	His	Pro	Tyr	Phe	Asn	Gln
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Arg	Lys	Leu	Leu	Asp	Phe	Cys	Lys	Ser	Lys	Asp	Ile	Val	Leu	Val	Ala
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Tyr	Ser	Ala	Leu	Gly	Ser	His	Arg	Glu	Glu	Pro	Trp	Val	Asp	Pro	Asn
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Ser	Pro	Val	Leu	Leu	Glu	Asp	Pro	Val	Leu	Cys	Ala	Leu	Ala	Lys	Lys
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His	Lys	Arg	Thr	Pro	Ala	Leu	Ile	Ala	Leu	Arg	Tyr	Gln	Leu	Gln	Arg
	290					295					300				
Gly	Val	Val	Val	Leu	Ala	Lys	Ser	Tyr	Asn	Glu	Gln	Arg	Ile	Arg	Gln
305					310					315					320
Asn	Val	Gln	Val	Phe	Glu	Phe	Gln	Leu	Thr	Ser	Glu	Glu	Met	Lys	Ala
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Ile	Asp	Gly	Leu	Asn	Arg	Asn	Val	Arg	Tyr	Leu	Thr	Leu	Asp	Ile	Phe
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<210> 173
<211> 1988
<212> DNA
<213> Homo sapiens
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<400> 173						
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<210> 174
<211> 238
<212> PRT
<213> Homo sapiens
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Leu Ser Ala Ile Ala Phe Asp Ile Ile Ala Leu Ala Gly Arg Gly Trp		
65	70	75 80
Leu Gln Ser Ser Asp His Gly Gln Thr Ser Ser Leu Trp Trp Lys Cys		
	85	90 95
Ser Gln Glu Gly Gly Gly Ser Gly Ser Tyr Glu Glu Gly Cys Gln Ser		
	100	105 110
Leu Met Glu Tyr Ala Trp Gly Arg Ala Ala Ala Ala Met Leu Phe Cys		
	115	120 125
Gly Phe Ile Ile Leu Val Ile Cys Phe Ile Leu Ser Phe Phe Ala Leu		
	130	135 140
Cys Gly Pro Gln Met Leu Val Phe Leu Arg Val Ile Gly Gly Leu Leu		
145	150	155 160
Ala Leu Ala Ala Val Phe Gln Ile Ile Ser Leu Val Ile Tyr Pro Val		
	165	170 175
Lys Tyr Thr Gln Thr Phe Thr Leu His Ala Asn Pro Ala Val Thr Tyr		
	180	185 190
Ile Tyr Asn Trp Ala Tyr Gly Phe Gly Trp Ala Ala Thr Ile Ile Leu		
	195	200 205
Ile Gly Cys Ala Phe Phe Phe Cys Cys Leu Pro Asn Tyr Glu Asp Asp		
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Leu Leu Gly Asn Ala Lys Pro Arg Tyr Phe Tyr Thr Ser Ala		
225	230	235

&lt;210&gt; 175

&lt;211&gt; 4181

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; unsure

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&lt;221&gt; unsure

&lt;222&gt; (3502)

&lt;223&gt; n=A,T,C or G

&lt;221&gt; unsure

&lt;222&gt; (3506)

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gctaagaaat aattcnataa ttgagttttg tactcnccaa anatgggtca ttcctcatgn 4080
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atcatttagg tccccaaaaa aaaaaaaaaa aaaaaaaaaa a

4181

<210> 176

<211> 580

<212> PRT

<213> Homo sapiens

<400> 176

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5 10 15

Asp Leu Glu Ser Ile Phe Lys Asp Ala Lys Ile Pro Val Ser Gly Pro  
20 25 30

Phe Leu Val Lys Thr Gly Tyr Ala Phe Val Asp Cys Pro Asp Glu Ser  
35 40 45

Trp Ala Leu Lys Ala Ile Glu Ala Leu Ser Gly Lys Ile Glu Leu His  
50 55 60

Gly Lys Pro Ile Glu Val Glu His Ser Val Pro Lys Arg Gln Arg Ile  
65 70 75 80

Arg Lys Leu Gln Ile Arg Asn Ile Pro Pro His Leu Gln Trp Glu Val  
85 90 95

Leu Asp Ser Leu Leu Val Gln Tyr Gly Val Val Glu Ser Cys Glu Gln  
100 105 110

Val Asn Thr Asp Ser Glu Thr Ala Val Val Asn Val Thr Tyr Ser Ser  
115 120 125

Lys Asp Gln Ala Arg Gln Ala Leu Asp Lys Leu Asn Gly Phe Gln Leu  
130 135 140

Glu Asn Phe Thr Leu Lys Val Ala Tyr Ile Pro Asp Glu Met Ala Ala  
145 150 155 160

Gln Gln Asn Pro Leu Gln Gln Pro Arg Gly Arg Arg Gly Leu Gly Gln  
165 170 175

Arg Gly Ser Ser Arg Gln Gly Ser Pro Gly Ser Val Ser Lys Gln Lys  
180 185 190

Pro Cys Asp Leu Pro Leu Arg Leu Leu Val Pro Thr Gln Phe Val Gly  
195 200 205

Ala Ile Ile Gly Lys Glu Gly Ala Thr Ile Arg Asn Ile Thr Lys Gln  
210 215 220

Thr Gln Ser Lys Ile Asp Val His Arg Lys Glu Asn Ala Gly Ala Ala  
225 230 235 240

Glu Lys Ser Ile Thr Ile Leu Ser Thr Pro Glu Gly Thr Ser Ala Ala  
245 250 255

Cys Lys Ser Ile Leu Glu Ile Met His Lys Glu Ala Gln Asp Ile Lys  
 260 265 270

Phe Thr Glu Glu Ile Pro Leu Lys Ile Leu Ala His Asn Asn Phe Val  
 275 280 285

Gly Arg Leu Ile Gly Lys Glu Gly Arg Asn Leu Lys Lys Ile Glu Gln  
 290 295 300

Asp Thr Asp Thr Lys Ile Thr Ile Ser Pro Leu Gln Glu Leu Thr Leu  
 305 310 315 320

Tyr Asn Pro Glu Arg Thr Ile Thr Val Lys Gly Asn Val Glu Thr Cys  
 325 330 335

Ala Lys Ala Glu Glu Glu Ile Met Lys Lys Ile Arg Glu Ser Tyr Glu  
 340 345 350

Asn Asp Ile Ala Ser Met Asn Leu Gln Ala His Leu Ile Pro Gly Leu  
 355 360 365

Asn Leu Asn Ala Leu Gly Leu Phe Pro Pro Thr Ser Gly Met Pro Pro  
 370 375 380

Pro Thr Ser Gly Pro Pro Ser Ala Met Thr Pro Pro Tyr Pro Gln Phe  
 385 390 395 400

Glu Gln Ser Glu Thr Glu Thr Val His Gln Phe Ile Pro Ala Leu Ser  
 405 410 415

Val Gly Ala Ile Ile Gly Lys Gln Gly Gln His Ile Lys Gln Leu Ser  
 420 425 430

Arg Phe Ala Gly Ala Ser Ile Lys Ile Ala Pro Ala Glu Ala Pro Asp  
 435 440 445

Ala Lys Val Arg Met Val Ile Ile Thr Gly Pro Pro Glu Ala Gln Phe  
 450 455 460

Lys Ala Gln Gly Arg Ile Tyr Gly Lys Ile Lys Glu Glu Asn Phe Val  
 465 470 475 480

Ser Pro Lys Glu Glu Val Lys Leu Glu Ala His Ile Arg Val Pro Ser  
 485 490 495

Phe Ala Ala Gly Arg Val Ile Gly Lys Gly Gly Lys Thr Val Asn Glu  
 500 505 510

Leu Gln Asn Leu Ser Ser Ala Glu Val Val Val Pro Arg Asp Gln Thr  
 515 520 525

Pro Asp Glu Asn Asp Gln Val Val Val Lys Ile Thr Gly His Phe Tyr  
 530 535 540

Ala Cys Gln Val Ala Gln Arg Lys Ile Gln Glu Ile Leu Thr Gln Val  
 545 550 555 560

Lys Gln His Gln Gln Gln Lys Ala Leu Gln Ser Gly Pro Pro Gln Ser  
 565 570 575

Arg Arg Lys

<210> 177

<211> 401

<212> DNA

<213> Homo sapiens

<400> 177

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atgccccgta aatgtcttca gtgttcttca gggtagttgg gatctcaaaa gatttggttc 60
agatccaaac aaatacacat tctgtgtttt agctcagtgt tttctaaaaa aagaaactgc 120
cacacagcaa aaaattgttt actttgttgg acaaaccaaa tcagttctca aaaaatgacc 180
gggtgcttata aaaagttata aatatcgagt agctctaaaa caaaccacct gaccaagagg 240
gaagtgaact tgtgcttagt atttacattg gatgccagtt ttgtaatcac tgacttatgt 300
gcaaactggg gcagaaattc tataaactct ttgctgtttt tgatacctgc tttttgtttc 360
attttgtttt gttttgtaaa aatgataaaa cttcagaaaa t 401
```

<210> 178

<211> 561

<212> DNA

<213> Homo sapiens

<400> 178

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acgcctttca aggggtgtacg caaagcactc attgataccc ttttggatgg ctatgaaaca 60
gcccgtatg ggacaggggt ctttggccag aatgagtacc tacgctatca ggaggccctg 120
agtgaactgg ccactgcggg taaagcacga attgggagct ctcagcgaca tcaccagtca 180
gcagccaaag acctaactca gtcccttgag gtctcccaa caaccatcca ggtgacatac 240
ctcccttcca gtcagaagag taaacgtgcc aagcacttcc ttgaattgaa gagctttaag 300
gataactata acacattgga gactactctg tgacggagct gaaggactct tgccgtagat 360
taagccagtc agttgcaatg tgcaagacag gctgcttgcc gggccgacct cggaacatct 420
ggcccagcag gccagactg taccatcca agttccggt gtatccagag ttcttagagc 480
ttgtgtctaa agggtaattc cccaacctt ccttatgagc attttttagaa cattggctaa 540
gactattttc cccagtagc g 561
```

<210> 179

<211> 521

<212> DNA

<213> Homo sapiens

<400> 179

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cccaacgcgt ttgcaaatat tcccctggta gcctacttcc ttacccccga atattggtaa 60
gatcgagcaa tggcttcagg acatgggttc tcttctcttg tgatcattca agtgctcact 120
gcatgaagac tggcttgtct cagtgtttca acctcaccag ggctgtctct tgggtccacac 180
ctcgtccctt gttagtgcg tatgacagcc cccatcaaatt gaccttggcc aagtcacggg 240
ttctctgtgg tcaagggttg ttggctgatt ggtggaaagt aggggtggacc aaaggaggcc 300
acgtgagcag tcagcaccag ttctgcacca gcagcgctc cgtcctagtg ggtgttctct 360
tttctctctg ccctgggttg gctagggcct gattcgggaa gatgcctttg caggaggagg 420
aggataagtg ggatctacca attgattctg gcaaaacaat ttctaagatt tttttgcttt 480
```



atgtgggaaa cagatctaaa tctcatttta tgctgtattt t

521

<210> 180

<211> 417

<212> DNA

<213> Homo sapiens

<400> 180

ggtggaattc gccgaagatg gcggaggtgc aggtccttgg gcttgatggc cgaggccatc 60  
 tcttgggccc cctggcgcc atcgtggcta aacaggtaact gctgggccc aaggagggtg 120  
 tcgtacgctg tgaaggcatc aacattttctg gcaattttcta cagaacaag ttgaagtacc 180  
 tggcttttct ccgcaagcgg atgaacacca acccttccc agggccctac cacttccggg 240  
 ccccgagccg catcttcttg cggaaccgtg gaggtatgct gcccacaaa accaagcgag 300  
 gccaggccgc tctggaccgt ctcaagggtg ttgacggcat cccaccgcc tacgacaaga 360  
 aaaagcggat ggtggttctt gctgccctca aggtcgtgctg tctgaagcct acaagaa 417

<210> 181

<211> 283

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (35)

<223> n=A,T,C or G

<400> 181

gattttcttct aaataggatg taaaacttct ttcanattac tcttctcag tctgacctgc 60  
 caagaactca agtgtaactg tgataaaaata acctttccca ggtatattgg caggtagtg 120  
 tgtaattctca gaatacacag gtgacataga tatgatatga caactggtaa tggtaggttc 180  
 atttacattg tttaacttct tatgaccagg ccttaaggga aggtcagttt tttaaaaaac 240  
 caagtagtgt cttcctacct atctccagat acatgtcaaa aaa 283

<210> 182

<211> 401

<212> DNA

<213> Homo sapiens

<400> 182

atattcttgc tgcttatgca gctgacattg ttgccctccc taaagcaacc aagtagcctt 60  
 tatttcccac agtgaaaagaa aacgctggcc tatcagttac attacaaaag gcagatttca 120  
 agaggattga gtaagtagtt ggatggcttt cataaaaaaca agaattcaag aagaggattc 180  
 atgctttaag aaacatttgt tatacattcc tcacaaatta tacctgggat aaaaactatg 240  
 tagcaggcag tgtgttttcc ttccatgtct ctctgcacta cctgcagtgt gtcctctgag 300  
 gctgcaagtc tgtcctatct gaattcccag cagaagcact aagaagctcc accctatcac 360  
 ctacagata aaactatggg gaaaacttaa atctgtgcat a 401

<210> 183

<211> 366

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (325)

<223> n=A,T,C or G

<400> 183

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accatcatgc tttgatgttc ccctgtcttt ctctcttctg ctctcaagag caaagggttaa 120
tttaaggaca aagatgaagt cactgtaaac taatctgtca ttgtttttac ctcccttttc 180
tttttcagtg cagaaattaa aagtaagtat aaagcaccgt gattgggagt gtttttgctg 240
gtgtcggaat cactggtaaa tgttggctga gaacaatccc tccccttgca cttgtgaaaa 300
cactttgagc gctttaagag attancctga gaaataatta aatatctttt ctcttcaaaa 360
aaaaaa 366
```

<210> 184

<211> 370

<212> DNA

<213> Homo sapiens

<400> 184

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tcttacttca aaagaaaaat aaacataaaa aataagttgc tggttcctaa caggaaaaat 60
tttaataatt gtactgagag aaactgctta cgtacacatt gcagatcaaa tatttgaggt 120
taaaatgtta gtctacatag atgggtgatt gtaactttat tgccattaaa agatttcaaa 180
ttgcattcat gcttctgtgt acacataatg aaaaatgggc aaataatgaa gatctctcct 240
tcagtctgct ctgtttaatt ctgctgtctg ctcttctcta atgctgcgtc cctaattgta 300
cacagtttag tgatatctag gagtataaag ttgtcgccca tcaataaaaa tcacaaagtt 360
ggtttaaaaa 370
```

<210> 185

<211> 107

<212> DNA

<213> Homo sapiens

<400> 185

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ctcatattat tttccttttg agaaattgga aactctttct gttgctatta tattaataaa 60
gttgggtgtt attttctggt agtcaccttc cccatttaaa aaaaaaa 107
```

<210> 186

<211> 309

<212> DNA

<213> Homo sapiens

<400> 186

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gaaaggatgg ctctgggttg cacagagctg ggacttcatg ttcttctaga gagggccaca 60
agagggccac aggggtggcc gggagttgtc agctgatgcc tgctgagagg caggaattgt 120
gccagtgagt gacagtcatg agggagtgtc tcttcttggg gaggaagaa ggtagagcct 180
ttctgtctga atgaaaggcc aaggctacag tacagggccc cgccccagcc aggggtgttaa 240
tgcccacgta gtggaggcct ctggcagatc ctgcattcca aggtcactgg actgtacgtt 300
tttatgggt 309
```

<210> 187

<211> 477

<212> DNA

<213> Homo sapiens

<400> 187

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ttcagtccta gcaagaagcg agaattctga gatcctccag aaagtcgagc agcaccacc 60
tccaacctcg ggccagtgtc ttcaggcttt actggggacc tgcgagctgg cctaattgtg 120
```

```

tggcctgcaa gccaggccat ccctgggccc cacagacgag ctccgagcca ggtcaggctt 180
cggaggccac aagctcagcc tcaggcccag gcaactgattg tggcagaggg gccactaccc 240
aaggtctagc taggcccag acctagttac ccagacagtg agaagcccct ggaaggcaga 300
aaagttggga gcatggcaga caggggaagg aaacattttc agggaaaaga catgtatcac 360
atgtcttcag aagcaagtca ggtttcattgt aaccgagtggt cctcttgctg gtccaaaagt 420
agcccagggc tgtagcacag gcttcacagt gattttgtgt tcagccgtga gtcacac 477

```

&lt;210&gt; 188

&lt;211&gt; 220

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 188

```

taaatatggg agatattaat attcctctta gatgaccagt gattccaatt gtcccaagtt 60
ttaaataagt accctgtgag tatgagataa attagtgaca atcagaacaa gtttcagtat 120
cagatgttca agaggaagtt gctattgcat tgattttaat atttgtagat aaacactgat 180
ttttttgagc attattttgt atttggtgta cttaataacc 220

```

&lt;210&gt; 189

&lt;211&gt; 417

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (76)

&lt;223&gt; n=A,T,C or G

&lt;221&gt; unsure

&lt;222&gt; (77)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 189

```

accatcttga cagaggatac atgctcccaa aacgtttgtt accacactta aaaatcactg 60
ccatcattaa gcatcnnttt caaaattata gccattcatg atttactttt tccagatgac 120
tatcattatt ctatgccttt gaatttgtaa ggggaaaaaa aacaaaaaca aaaacttacg 180
atgcactttt ctccagcaca tcagatttca aattgaaaat taaagacatg ctatggtaat 240
gcacttgcta gtactacaca ctttgtacaa caaaaaacag aggcaagaaa caacggaaaag 300
agaaaagcct tcctttgttg gcccttaaac tgagtcaaga tctgaaatgt agagatgatc 360
tctgacgata cctgtatgtt cttattgtgt aaataaaatt gctggtatga aatgaca 417

```

&lt;210&gt; 190

&lt;211&gt; 497

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 190

```

gcaactgcgg gctctcccgt cccgcggtgg ttgctgctgc tgccgctgct gctgggcctg 60
aacgcaggag ctgtcattga ctggcccaca gaggagggca aggaagtatg ggattatgtg 120
acggtccgca aggatgccta catgttcttg tggctctatt atgccaccaa ctctgcaag 180
aacttctcag aactgcccct ggtcatgtgg cttcagggag gtccaggcgg ttctagcact 240
ggatttgga aacttgagga aattggggcc cttgacagtg atctcaaacc acggaaaacc 300
acctggctcc aggctgccag tctcctattt gtggataatc ccgtgggcac tgggttcagt 360
tatgtgaatg gtagtggtgc ctatgccaaag gacctggcta tgggtggctc agacatgatg 420
gttctcctga agaccttctt cagttgccac aaagaattcc agacagttcc attctacatt 480
ttctcagagt cctatgg 497

```

<210> 191  
<211> 175  
<212> DNA  
<213> Homo sapiens

<400> 191  
atgttgaata ttttgcttat taactttggt tattgtcttc tccctcgatt agaattattag 60  
ctacttgagt acaaggattt gagcctgtta cattcactgc tgaatttttag gtccttgga 120  
gatacccagc attcaataga gaccacacaa taaatatatg tcaaataaaa aaaaa 175

<210> 192  
<211> 526  
<212> DNA  
<213> Homo sapiens

<400> 192  
agtaaacatt attatTTTTT ttatatTTTgc aaaggaaaca tatctaattcc ttcctataga 60  
agaacagta ttgctgtaat tcctTTTTctt ttcttctctca tttcctctgc cccttaaaag 120  
attgaagaaa gagaaacttg tcaactcata tccacgttat ctagcaaagt acataagaat 180  
ctatcactaa gtaatgtatc cttcagaatg tggttggttta ccagtgcacac cccatattca 240  
tcacaaaatt aaagcaagaa gtccatagta atttatTTTgc taatagtga tttttaatgc 300  
tcagagtttc tgaggtcaaa ttttatcttt tcacttaca gctctatgat cttaaataat 360  
ttacttaatg tattttggtg tattttctct aaattaatat tgggtgttcaa gactatatct 420  
aattcctctg atcactttga gaaacaaact tttattaaat gtaaggcact tttctatgaa 480  
ttttaaatat aaaaataaat attgtttctga ttattactga aaaaaa 526

<210> 193  
<211> 553  
<212> DNA  
<213> Homo sapiens

<220>  
<221> unsure  
<222> (290)  
<223> n=A,T,C or G  
<221> unsure  
<222> (300)  
<223> n=A,T,C or G  
<221> unsure  
<222> (411)  
<223> n=A,T,C or G  
<221> unsure  
<222> (441)  
<223> n=A,T,C or G

<400> 193  
tccattgtgg tggaattcgc tctctggtaa aggcgtgcag gtggtggccg cggcctctga 60  
gctgggatga gccgtgctcc cgggtggaagc aaggagagccc agccggagcc atggccagta 120  
cagtggtagc agttggactg accattgctg ctgcaggatt tgcaggccgt tacgttttgc 180  
aagccatgaa gcatatggag cctcaagtaa aacaagtttt tcaaagccta ccaaaatctg 240  
ccttcagtgg tggtattat agaggtgggt ttgaacccaa aatgacaaan cgggaagcan 300  
cattaatact aggtgtaagc cctactgcc aataagggaa aataagagat gctcatcgac 360  
gaattatgct tttaaatcat cctgacaaag gaggatctcc ttatatagca nccaaaatca 420  
atgaagctaa agatttacta naaggtcaag ctaaaaaatg aagtaaattg atgatgaatt 480

ttaagttcgt attagtttat gtatatgagt actaagtttt tataataaaa tgcctcagag 540  
ctacaatttt aaa 553

<210> 194

<211> 320

<212> DNA

<213> Homo sapiens

<400> 194

cccttcccaa tccatcagta aagaccccat ctgccttgtc catgccgttt cccaacaggg 60  
atgtcacttg atatgagaat ctcaaatctc aatgccttat aagcattcct tctgtgtgcc 120  
attaagactc tgataattgt ctccccctca taggaatttc tcccaggaaa gaaatatatc 180  
cccatctccg tttcatatca gaactaccgt ccccgatatt cccttcagag agattaaaga 240  
ccagaaaaaa gtgagcctct tcatctgcac ctgtaatagt ttcagttcct attttcttcc 300  
attgacccat atttatacct 320

<210> 195

<211> 320

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (203)

<223> n=A,T,C or G

<221> unsure

<222> (218)

<223> n=A,T,C or G

<400> 195

aagcatgacc tggggaaatg gtcagacctt gtatttgtgt tttggccttg aaagtagcaa 60  
gtgaccagaa tctgccatgg caacaggctt taaaaaagac ccttaaaaag acactgtctc 120  
aactgtggtg ttagcaccag ccagctctct gtacatttgc tagcttgtag ttttctaaga 180  
ctgagtaaac ttcttatttt tanaaaaggg aggctggnnt gtaactttcc ttgtacttaa 240  
ttgggtaaaa gtctttttcca caaaccacca tctattttgt gaactttgtt agtcactctt 300  
tatttggtaa attatgaact 320

<210> 196

<211> 357

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (36)

<223> n=A,T,C or G

<400> 196

atataaaata atacgaaact ttaaaaagca ttggantgtc agtatgttga atcagtagtt 60  
tcactttaac tgtaaacaat ttcttaggac accatttggg ctagtttctg tgtaagtgtg 120  
aatactacaa aaacttatatt atactgttct tatgtcattt gttatattca tagatttata 180  
tgatgatatg acatctggct aaaaagaaat tattgcaaaa ctaaccacta tgtacttttt 240  
tataaatact gtatggacaa aaaatggcat tttttatatt aaattgttta gctctggcaa 300  
aaaaaaaaa ttttaagagc tgggtactaat aaaggattat tatgactgtt aaaaaaa 357

<210> 197  
 <211> 565  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> (27)  
 <223> n=A,T,C or G

<400> 197  
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 aagcaacaat acttcctctt gacagctttg attggaatgg ggttattaga tcattcacct 120  
 tggtcctaca ctttttagga tgcttgggtga acataacacc acttataatg aacatccctg 180  
 gttcctatat tttgggctat gtgggtagga attgttactt gttactgcag cagcagccct 240  
 agaaagtaag cccagggtct cagatctaag ttagtccaaa agctaaatga tttaaagtca 300  
 agttgtaatg ctaggcataa gcaactctata atacattaaa ttataggccg agcaattagg 360  
 gaatgtttct gaaacattaa acttggtatt atgtcactaa aattctaaca caaacttaaa 420  
 aaatgtgtct catacatatg ctgtactagg cttcatcatg catttctaaa tttgtgtatg 480  
 atttgaatat atgaaagaat ttatacaaga gtgttattta aaattattaa aaataaatgt 540  
 atataatttg tacctattgt aaaaa 565

<210> 198  
 <211> 484  
 <212> DNA  
 <213> Homo sapiens

<400> 198  
 tatgtaagta ttggtgtctg ctttaaaaaa ggagaccag acttcacctg tccttttttaa 60  
 acatttgaga acagtgttac tctgagcagt tggggccacct tcaccttatc cgacagctga 120  
 ctgttggatg tgtccattgt cggcagtttg gctgttgccc ggacaggaca ggacctccat 180  
 tgggcgcagc agcagggtggc aggggtgtgg cttgagggtg gtggcagcgt ctggtcctcc 240  
 tctctggtgc tttctgagag ggtctctaaa gcagagtgtg gttggcctgg gggaaggcag 300  
 agcacgtatt tctccctct agtacctctg catttgtgag tgttccctct ggctttctga 360  
 agggcagcag actcttgagt atactgcaga ggacatgctt tatcagtagg tcctgagggc 420  
 tccaggggct caactgacca agtaacacag aagttggggg atgtggccta tttgggtcgg 480  
 aaac 484

<210> 199  
 <211> 429  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> (77)  
 <223> n=A,T,C or G  
 <221> unsure  
 <222> (88)  
 <223> n=A,T,C or G  
 <221> unsure  
 <222> (134)  
 <223> n=A,T,C or G  
 <221> unsure  
 <222> (151)

<223> n=A,T,C or G  
 <221> unsure  
 <222> (189)  
 <223> n=A,T,C or G  
 <221> unsure  
 <222> (227)  
 <223> n=A,T,C or G  
 <221> unsure  
 <222> (274)  
 <223> n=A,T,C or G  
 <221> unsure  
 <222> (319)  
 <223> n=A,T,C or G

<400> 199

```
gcttatgttt tttgttttaa cttttgtttt ttaacattta gaatattaca ttttgtatta 60
tacagtacct ttctcanaca ttttgtanaa ttcatttcgg cagctcacta ggattttgct 120
gaacattaaa aagngtgata gcgatattag ngccaatcaa atggaaaaaa ggtagtctta 180
ataaacaana cacaacgttt ttatacaaca tactttaaaa tattaanaaa actccttaat 240
attgtttcct attaatgtatt attctttggg caanattttc tgatgctttt gattttctct 300
caatttagca tttgctttng gtttttttct ctatttagca ttctgttaag gcacaaaaac 360
tatgtactgt atgggaaatg ttgtaaatat taccttttcc acatttttaa cagacaactt 420
tgaatccaa 429
```

<210> 200

<211> 279

<212> DNA

<213> Homo sapiens

<400> 200

```
gcttttttga ggaattacag ggaagctcct ggaattgtac atggatatct ttatccctag 60
ggggaaatca aggagctggg caccctaat tctttatgga agtgttttaa actattttta 120
ttttattaca agtattacta gagtagtggg tctactctaa gatttcaaaa gtgcatttaa 180
aatcatatcat gttcccgctt gcaaatatat tgttattttg gtggagaaaa aaatagtata 240
ttctacataa aaaattaaag atattaacta agaaaaaaa 279
```

<210> 201

<211> 569

<212> DNA

<213> Homo sapiens

<400> 201

```
taggtcagta ttttttagaaa ctcttaatat ctcatactct tgataccaaa agcagccctg 60
attgtttaaag cacacacctg cacaagaagc agtgatgggt gcattttacat ttcctgggtg 120
cacaaaaaaa aattctcaaa aagcaaggac ttacgctttt tgcaaagcct ttgagaagtt 180
actggatcat aggaagctta taacaagaat ggaagattct taaataactc actttctttg 240
gtatccagta acagtagatg ttcaaaatat gtagctgatt aataaccagca ttgtgaacgc 300
tgtacaacct tgtggttatt actaagcaag ttactactag cttctgaaaa gtagcttcat 360
aattaatgtt atttatacac tgccctccat gacttttact ttgccctaag ctaatctcca 420
aaatctgaaa tgctactcca atatcagaaa aaaaggggga ggtggaatta tatttcctgt 480
gatttttaaga gtacagagaa tcatgcacat ctctgattag ttcatatatg tctagtgtgt 540
aataaaagtc aaagatgaac tctcaaaaa 569
```

<210> 202

<211> 501

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 202

```

attaataggc ttaataattg ttggcaagga tccttttgct ttctttggca tgcaagctcc 60
tagcatctgg cagtggggcc aagaaaataa ggtttatgca tgtatgatgg tttcttctt 120
gagcaacatg attgagaacc agtgtatgtc aacaggtgca tttgagataa ctttaaataga 180
tgtacctgtg tggctctaagc tggaatctgg tcacctcca tccatgcaac aacttgttca 240
aattcttgac aatgaaatga agctcaatgt gcatatggat tcaatccac accatcgatc 300
atagcaccac ctatcagcac tgaaaactct tttgcattaa gggatcattg caagagcagc 360
gtgactgaca ttatgaaggc ctgtactgaa gacagcaagc tgtagtaca gaccagatgc 420
ttctttggca ggctcgttgt acctcttggg aaacctcaat gcaagatagt gtttcagtgc 480
tggcatattt tgggaattctg c                                     501

```

&lt;210&gt; 203

&lt;211&gt; 261

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (36)

&lt;223&gt; n=A,T,C or G

&lt;221&gt; unsure

&lt;222&gt; (96)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 203

```

gacaagctcc tggctcttgag atgtcttctc gttaangaga tgggcctttt ggaggtaaag 60
gataaaatga atgagttctg tcatgattca ctattntata acttgcatga cttttactgt 120
gttagctctt tgaatgttct tgaaatttta gactttcttt gtaaacaat gatatgtcct 180
tatcattgta taaaagctgt tatgtgcaac agtgtggaga ttccttgtct gatttaataa 240
aataacttaa cactgaaaaa a                                     261

```

&lt;210&gt; 204

&lt;211&gt; 421

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 204

```

agcatctttt ctacaacgtt aaaattgcag aagtagctta tcattaataa acaacaacaa 60
caacaataac aataaatcct aagtgtaaat cagttattct accccctacc aaggatatca 120
gcctgttttt tccctttttt ctccctggga taattgtggg cttcttccca aatttctaca 180
gcctctttcc tcttctcatg cttgagcttc cctgtttgca cgcattgctg tgcaggactg 240
gcttgtgtgc ttggactcgg ctccaggtgg aagcatgctt tcccttgta ctgttgga 300
aactcaaacc ttcaagccct aggtgtagcc attttgtcaa gtcattcaact gtatttttgt 360
actggcatta acaaaaaaag aagataaat attgtaccat taaactttaa taaaacttta 420
a                                     421

```

&lt;210&gt; 205

&lt;211&gt; 460

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 205



```
tactctcaca atgaaggacc tggaatgaaa aatctgtgtc taaacaagtc ctcttttagat 60
tttagtgcaa atccagagcc agcgtcgggt gcctcgagta attctttcat gggtagcttt 120
ggaaaagctc tcaggagacc tcacctagat gcctattcaa gctttggaca gccatcagat 180
tgtcagccaa gagcctttta ttgaaaagct cattcttccc cagacttgga ctctgggtca 240
gaggaagatg ggaaagaaaag gacagatttt caggaagaaa atcacatttg tacctttaaa 300
cagactttag aaaactacag gactccaaat tttcagtcct atgacttgga cacatagact 360
gaatgagacc aaaggaaaaag cttaacatac tacctcaagg tgaactttta tttaaaagag 420
agagaatctt atgtttttta aatggagtta tgaattttta 460
```

&lt;210&gt; 206

&lt;211&gt; 481

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 206

```
tgtggtggaa ttcgggacgc cccagagacc tgactttttc ctgctggggc cgtctctccc 60
tgcggaagca gtgacctctg acccctgggtg accttcgctt tgagtgcctt ttgaacgctg 120
gtcccgcggg acttggtttt ctcaagctct gtctgtccaa agacgctccg gtcgaggtcc 180
cgcttgcctt ggggtggatac ttgaacccca gacgcccctc tgtgtgtgtg tgtccggagg 240
cggccttccc atctgcctgc ccaccggag ctctttccgc cggcgcaggg tcccaagccc 300
acctccgcgc ctcatctctg cgggtgtgct ctgggcacgt cctgcacaca caatgcaagt 360
cctggcctcc gcgcccgcgc gccacgcga gccgtaccgc ccgccaactc tgttatttat 420
ggtgtgaccc cctggagggtg ccctcgcccc accggggcta tttattgttt aatttatttg 480
t 481
```

&lt;210&gt; 207

&lt;211&gt; 605

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 207

```
accttttttg gattcagggc tcctcacaat taaaatgagt gtaatgaaac aaggtgaaaa 60
tatagaagca tccctttgta tactgttttg ctacttacag tgtacttggc attgctttat 120
ctcactggat tctcacggta ggattttctga gatcttaatc taagctccaa agttgtctac 180
ttttttgate ctagggtgct ctttttgttt tacagagcag ggtcacttga tttgctagct 240
ggtggcagaa ttggcaccat taccaggtc tgactgacca ccagtcagag gcactttatt 300
tgtatcatga aatgatttga aatcatttga aagcagcgaa gtctgataat gaatgccagc 360
tttccttgtg ctttgataac aaagactcca aatattcttg agaacctgga taaaagtttg 420
aagggctaga ttgggatttg aagacaaaat tgtaggaaat cttacatttt tgcaataaca 480
aacattaatg aaagcaaaac attataaaag taattttaat tcaccacata cttatcaatt 540
tcttgatgct tccaaatgac atctaccaga tatggttttg tggacatctt tttctgttta 600
cataa 605
```

&lt;210&gt; 208

&lt;211&gt; 655

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 208

```
ggcgttggtc tggattcccg tcgtaactta aagggaaact ttcacaatgt ccggagccct 60
tgatgtcctg caaatgaagg aggaggatgt ccttaagttc cttgcagcag gaaccacttt 120
agggtggcacc aatcttgact tccagatgga acagtacatc tataaaagga aaagtgatgg 180
catctatatc ataaatctca agaggacctg ggagaagctt ctgctggcag ctctgtgcaat 240
tgttgccatt gaaaaccctg ctgatgtcag tgttatatcc tccaggaata ctggccagag 300
ggctgtgctg aagtttgctg ctgccactgg agccactcca attgctggcc gcttcactcc 360
```

```

tggaaccttc actaaccaga tccaggcagc cttccgggag ccacggcttc ttgtgggttac 420
tgaccccagg gctgaccacc agcctctcac ggaggcatct tatgttaacc tacctaccat 480
tgcgctgtgt aacacagatt ctctctcgcg ctatgtggac attgccatcc catgcaacaa 540
caagggagct cactcagtgg gtttgatgtg gtggatgctg gctcgggaag ttctgcgcat 600
gcgtggcacc atttcccgctg aacacccatg ggaggtcatg cctgatctgt acttc 655

```

<210> 209

<211> 621

<212> DNA

<213> Homo sapiens

<400> 209

```

catttagaac atggttatca tccaagacta ctctaccctg caacattgaa ctccaagag 60
caaatccaca ttctcttga gttctgcagc ttctgtgtaa atagggcagc tgcgtctat 120
gccgtagaat cacatgatct gaggaccatt catggaagct gctaaatagc ctagtctggg 180
gagtcttcca taaagttttg catggagcaa acaaacagga ttaaactagg tttggttcct 240
tcagccctct aaaagcatag ggcttagcct gcaggcttcc ttgggctttc tctgtgtgtg 300
tagttttgta aacactatag catctgttaa gatccagtgt ccatggaaac cttcccacat 360
gcogtgactc tggactatat cagttttttg aaagcagggt tcctctgcct gctaacaagc 420
ccacgtggac cagtctgaat gtctttcctt tacacctatg tttttaaata gtcaaacttc 480
aagaaacaat ctaaacaagt ttctgttgca tatgtgtttg tgaacttgta tttgtattta 540
gtaggcttct atattgcatt taacttgttt ttgtaactcc tgattcttcc ttttcggata 600
ctattgatga ataaagaaat t 621

```

<210> 210

<211> 533

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (20)

<223> n=A,T,C or G

<221> unsure

<222> (21)

<223> n=A,T,C or G

<221> unsure

<222> (61)

<223> n=A,T,C or G

<400> 210

```

cgccttgggg agccggcggn ngagtccggg acgtggagac ccgggggtccc ggcagccggg 60
ngggccgcgg gccaggggtg gggatgcacc gccgcgggggt gggagctggc gccatcgcca 120
agaagaaact tgcagaggcc aagtataagg agcgaggagc ggtcttggct gaggaccagc 180
tagcccagat gtcaaagcag ttggacatgt tcaagaccaa cctggaggaa tttgccagca 240
aacacaagca ggagatccgg aagaatcctg agttccgtgt gcagttccag gacatgtgtg 300
caaccattgg cgtggatccg ctggcctctg gaaaaggatt ttggtctgag atgctgggcg 360
tgggggactt ctattacgaa ctaggtgtcc aaattatcga agtgtgcctg gcgctgaagc 420
atcgggaatg aggtctgata actttggagg aactacatca acaggtgttg aagggaaggg 480
gcaagttcgc ccaggatgtc agtcaagatg acctgatcag agccatcaag aaa 533

```

<210> 211

<211> 451

<212> DNA

<213> Homo sapiens

&lt;400&gt; 211

```

ttagcttgag ccgagaacga ggcgagaaag ctggagaccg aggagaccgc ctagagcgga 60
gtgaacgggg aggggaccgt ggggaccggc ttgatcgtgc gcggacacct gctaccaagc 120
ggagcttcag caaggaaagt gaggagcgga gtagagaacg gccctcccag cctgaggggc 180
tgcgcaaggc agctagcctc acggaggatc gggaccgtgg gcgggatgcc gtgaagcgag 240
aagctgccct acccccagtg agccccctga aggcggctct ctctgaggag gagttagaga 300
agaaatccaa ggctatcatt gaggaatatc tccatctcaa tgacatgaaa gaggcagtcc 360
agtgcgtgca ggagctggcc tcaccctcct tgctcttcat ctttgtacgg catggtgtcg 420
agtctacgct ggagcgcagt gccattgctc g                                     451

```

&lt;210&gt; 212

&lt;211&gt; 471

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (54)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 212

```

gtgattattc ttgatcaggg agaagatcat ttagatttgt tttgcattcc ttanaatgga 60
gggcaacatt ccacagctgc cctggctgtg atgagtgtcc ttgcaggggc cggagtagga 120
gcaactgggt gggggcggaa ttgggggttac tcgatgtaag ggattccttg ttgttggtgt 180
gagatccagt gcagttgtga tttctgtgga tcccagcttg gttccaggaa ttttgtgtga 240
ttggcttaaa tccagttttc aatcttcyac agctgggctg gaacgtgaac tcagtagctg 300
aacctgtctg acccggtcac gttcttggtat cctcagaact ctttgcctct gtcggggtgg 360
gggtgggaac tcacgtgggg agcgggtggc gagaaaatgt aaggattctg gaatacatat 420
tccatgggac tttccttccc tctcctgctt cctcttttcc tgctccctaa c                                     471

```

&lt;210&gt; 213

&lt;211&gt; 511

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (27)

&lt;223&gt; n=A,T,C or G

&lt;221&gt; unsure

&lt;222&gt; (63)

&lt;223&gt; n=A,T,C or G

&lt;221&gt; unsure

&lt;222&gt; (337)

&lt;223&gt; n=A,T,C or G

&lt;221&gt; unsure

&lt;222&gt; (442)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 213

```

ctaattagaa acttgctgta ctttttnttt tcttttaggg gtcaaggacc ctctttatag 60
ctnccatttg cctacaataa attattgcag cagtttgcaa tactaaaata ttttttatag 120
actttatatt tttccttttg ataaagggat gctgcatagt agagtgggtg taattaaact 180
atctcagccg tttccctgct ttcccttctg ctccatatgc ctcatgtgcc ttccaggag 240

```

```

ctctttttaat cttaaagttc tacatttcat gctcttagtc aaattctggt accttttttaa 300
taactcttcc cactgcatat ttccatcttg aattggnggt tctaaattct gaaactgtag 360
ttgagataca gctattttaat atttctggga gatgtgcac cctcttcttt gtggttgccc 420
aaggttgttt tgcgtaactg anactccttg atatgcttca gagaatttag gcaaactg 480
gccatggccg tgggagtact gggagtaaaa t 511

```

&lt;210&gt; 214

&lt;211&gt; 521

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 214

```

agcattgcca aataatccct aattttccac taaaaatata atgaaatgat gttaagcttt 60
ttgaaaagtt taggttaaag ctactgttgt tagattaatg tatttggtgc ttccctttat 120
ctggaatgtg gcattagctt ttttatttta accctcttta attcttattc aattccatga 180
cttaagggtg gagagctaaa cactgggatt tttggataac agactgacag ttttgcataa 240
ttataatcgg cattgtacat agaaaggata tggctacctt ttgttaaadc tgcactttct 300
aaatatcaaa aaagggaaat gaagtataaa tcaatttttg tataatctgt ttgaaacatg 360
agttttatatt gcttaatat agggctttgc cccttttctg taagtctctt gggatcctgt 420
gtagaagctg ttctcattaa acaccaaaca gttaagtcca ttctctggta ctagctacaa 480
attcggtttc atattctact taacaattta aataaactga a 521

```

&lt;210&gt; 215

&lt;211&gt; 381

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (17)

&lt;223&gt; n=A,T,C or G

&lt;221&gt; unsure

&lt;222&gt; (20)

&lt;223&gt; n=A,T,C or G

&lt;221&gt; unsure

&lt;222&gt; (60)

&lt;223&gt; n=A,T,C or G

&lt;221&gt; unsure

&lt;222&gt; (61)

&lt;223&gt; n=A,T,C or G

&lt;221&gt; unsure

&lt;222&gt; (365)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 215

```

gagcggagag cggaccngtn agagccctga gcagccccac cgccgcccgc ggcctagttt 60
ncatcacacc ccgggaggag ccgcagctgc cgcagccggc cccagtcacc atcacgcaa 120
ccatgagcag cgaggccgag acccagcagc cgcccgcgcg ccccccgccg gcccccgccc 180
tcagcgcgcg cgacaccaag cccggcacta cgggcagcgg cgcagggagc ggtggcccg 240
gcggcctcac atcggcggcg cctgccggcg gggacaagaa ggtcatcgca acgaaggttt 300
tggaacagt aaaatggttc aatgtaagga acggatatgg tttcatcaac aggaatgaca 360
ccaangaaga tgtatttga c 381

```

&lt;210&gt; 216

&lt;211&gt; 425

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 216

```

ttactaacta ggtcattcaa ggaagtcaag ttaacttaaa catgtcacct aaatgcactt 60
gatgggtgtg aaatgtccac cttcttaaat ttttaagatg aacttagttc taaagaagat 120
aacaggccaa tcctgaaggt actccctggt tgctgcagaa tgtcagatat tttggatgtt 180
gcataagagt cctatttgcc ccagttaatt caacttttgt ctgcctgttt tgtggactgg 240
ctggctctgt tagaactctg tccaaaaagt gcatggaata taacttgtaa agcttcccac 300
aattgacaat atatatgcat gtgtttaaac caaatccaga aagcttaaac aatagagctg 360
cataatagta tttattaaag aatcacaaact gtaaacatga gaataactta aggattctag 420
tttag                                           425

```

&lt;210&gt; 217

&lt;211&gt; 181

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 217

```

gagaaaccaa atgatagggt gtagagcctg atgactccaa acaaagccat cccccgcatt 60
cttctcctt cttctgggtg tacagctcca agggcccttc accttcatgt ctgaaatgga 120
actttggcct tttcagtgga agaatatgtt gaaggtttca ttttgttcta gaaaaaaaaa 180
a                                           181

```

&lt;210&gt; 218

&lt;211&gt; 405

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 218

```

caggccttcc agttcactga caaacatggg gaagtgtgcc cagctggctg gaaacctggc 60
agtgatacca tcaagcctga tgtccaaaag agcaaagaat atttctccaa gcagaagtga 120
gcgctgggct gttttagtgc caggctgcgg tgggcagcca tgagaacaaa acctcttctg 180
tatttttttt ttccattagt aaaacacaag acttcagatt cagccgaatt gtggtgtctt 240
acaaggcagg cctttcctac aggggggtgga gagaccagcc tttcttcctt tggtaggaat 300
ggcctgagtt ggcgttgtgg gcaggctact ggtttgtatg atgtattagt agagcaaccc 360
attaatcttt tgtagtttgt attaaacttg aactgagaaa aaaaaa                    405

```

&lt;210&gt; 219

&lt;211&gt; 216

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (207)

&lt;223&gt; n=A,T,C or G

&lt;221&gt; unsure

&lt;222&gt; (210)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 219

```

actccaagag ttagggcagc agagtggagc gatttagaaa gaacatttta aaacaatcag 60
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tcaattgtaa acttcttggt aagactgtta cgtttctatt gcttttgtat gggatattgc 180

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aaaaataaaaa aggaaagaac cctcttnaan aaaaaa

216

<210> 220

<211> 380

<212> DNA

<213> Homo sapiens

<400> 220

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gcatgtaata atgttgagtg gcagtcaaaa gtcattgatt ttatcttagt tcttcattac 300
tgcattgaaa aggaaaacct gtctgagaaa atgcctgaca gtttaattta aaactatggt 360
gtaagtcttt gacaaaaaaa                                     380

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<210> 221

<211> 398

<212> DNA

<213> Homo sapiens

<400> 221

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gtgagtctgc aagtgaattt cactgatgtt gatattcatt gtgtgtagtt ttatttcggt 180
cccagccccg tttcctttta ttttggagct aatgccagct gcgtgtctag ttttgagtgc 240
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gtttctgtgg gagcagtgtg caccaactct tctgtatat tgcccttttg ctggaaaatg 360
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<210> 222

<211> 301

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (49)

<223> n=A,T,C or G

<221> unsure

<222> (64)

<223> n=A,T,C or G

<400> 222

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gatgacttta ggatttgcac ttttcccttt attgcctcat ttcttgtgac gccttggttg 240
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a                                                                 301

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<210> 223

<211> 200

<212> DNA

<213> Homo sapiens

&lt;400&gt; 223

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 agatttctac aggagacagt ggttttattt ggattgtctt ctgtaatagg tttcaataaa 180  
 gctggatgaa cttaaaaaaa 200

&lt;210&gt; 224

&lt;211&gt; 385

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 224

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 gctgtaactg caagacctgg acaagagatt cgtcagcgaa ctgcagctca aagaaacctt 120  
 tctccaacac cagcaagccc taaccagggc cctcctccac aagttccagt atctcctgga 180  
 ccaccaaagg acagttctgc ccctggtgga ccccccagaaa ggactgttac tccagcccta 240  
 tcatcaaagt tgttaccaag acatcttgga tccccgtcta cttcagtgcc tggaatgggt 300  
 aaacagagca cttaatgtta tttacagttt atattgtttt ctctggttac caataaaacg 360  
 ggccattttc aggtggtaaa aaaaa 385

&lt;210&gt; 225

&lt;211&gt; 560

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 225

Met	Glu	Cys	Leu	Tyr	Tyr	Phe	Leu	Gly	Phe	Leu	Leu	Leu	Ala	Ala	Arg	1	5	10	15
Leu	Pro	Leu	Asp	Ala	Ala	Lys	Arg	Phe	His	Asp	Val	Leu	Gly	Asn	Glu	20	25	30	
Arg	Pro	Ser	Ala	Tyr	Met	Arg	Glu	His	Asn	Gln	Leu	Asn	Gly	Trp	Ser	35	40	45	
Ser	Asp	Glu	Asn	Asp	Trp	Asn	Glu	Lys	Leu	Tyr	Pro	Val	Trp	Lys	Arg	50	55	60	
Gly	Asp	Met	Arg	Trp	Lys	Asn	Ser	Trp	Lys	Gly	Gly	Arg	Val	Gln	Ala	65	70	75	80
Val	Leu	Thr	Ser	Asp	Ser	Pro	Ala	Leu	Val	Gly	Ser	Asn	Ile	Thr	Phe	85	90	95	
Ala	Val	Asn	Leu	Ile	Phe	Pro	Arg	Cys	Gln	Lys	Glu	Asp	Ala	Asn	Gly	100	105	110	
Asn	Ile	Val	Tyr	Glu	Lys	Asn	Cys	Arg	Asn	Glu	Ala	Gly	Leu	Ser	Ala	115	120	125	
Asp	Pro	Tyr	Val	Tyr	Asn	Trp	Thr	Ala	Trp	Ser	Glu	Asp	Ser	Asp	Gly	130	135	140	
Glu	Asn	Gly	Thr	Gly	Gln	Ser	His	His	Asn	Val	Phe	Pro	Asp	Gly	Lys	145	150	155	160
Pro	Phe	Pro	His	His	Pro	Gly	Trp	Arg	Arg	Trp	Asn	Phe	Ile	Tyr	Val	165	170	175	
Phe	His	Thr	Leu	Gly	Gln	Tyr	Phe	Gln	Lys	Leu	Gly	Arg	Cys	Ser	Val	180	185	190	
Arg	Val	Ser	Val	Asn	Thr	Ala	Asn	Val	Thr	Leu	Gly	Pro	Gln	Leu	Met	195	200	205	
Glu	Val	Thr	Val	Tyr	Arg	Arg	His	Gly	Arg	Ala	Tyr	Val	Pro	Ile	Ala				

210		215		220
Gln Val Lys Asp Val Tyr Val Val Thr Asp Gln Ile Pro Val Phe Val				
225		230		235
Thr Met Phe Gln Lys Asn Asp Arg Asn Ser Ser Asp Glu Thr Phe Leu				240
	245		250	255
Lys Asp Leu Pro Ile Met Phe Asp Val Leu Ile His Asp Pro Ser His				
	260	265		270
Phe Leu Asn Tyr Ser Thr Ile Asn Tyr Lys Trp Ser Phe Gly Asp Asn				
	275	280		285
Thr Gly Leu Phe Val Ser Thr Asn His Thr Val Asn His Thr Tyr Val				
	290	295		300
Leu Asn Gly Thr Phe Ser Leu Asn Leu Thr Val Lys Ala Ala Ala Pro				
305		310		315
Gly Pro Cys Pro Pro Pro Pro Pro Pro Arg Pro Ser Lys Pro Thr				
	325		330	335
Pro Ser Leu Gly Pro Ala Gly Asp Asn Pro Leu Glu Leu Ser Arg Ile				
	340	345		350
Pro Asp Glu Asn Cys Gln Ile Asn Arg Tyr Gly His Phe Gln Ala Thr				
	355	360		365
Ile Thr Ile Val Glu Gly Ile Leu Glu Val Asn Ile Ile Gln Met Thr				
	370	375		380
Asp Val Leu Met Pro Val Pro Trp Pro Glu Ser Ser Leu Ile Asp Phe				
385		390		395
Val Val Thr Cys Gln Gly Ser Ile Pro Thr Glu Val Cys Thr Ile Ile				
	405		410	415
Ser Asp Pro Thr Cys Glu Ile Thr Gln Asn Thr Val Cys Ser Pro Val				
	420	425		430
Asp Val Asp Glu Met Cys Leu Leu Thr Val Arg Arg Thr Phe Asn Gly				
	435	440		445
Ser Gly Thr Tyr Cys Val Asn Leu Thr Leu Gly Asp Asp Thr Ser Leu				
	450	455		460
Ala Leu Thr Ser Thr Leu Ile Ser Val Pro Asp Arg Asp Pro Ala Ser				
465		470		475
Pro Leu Arg Met Ala Asn Ser Ala Leu Ile Ser Val Gly Cys Leu Ala				
	485		490	495
Ile Phe Val Thr Val Ile Ser Leu Leu Val Tyr Lys Lys His Lys Glu				
	500		505	510
Tyr Asn Pro Ile Glu Asn Ser Pro Gly Asn Val Val Arg Ser Lys Gly				
	515	520		525
Leu Ser Val Phe Leu Asn Arg Ala Lys Ala Val Phe Phe Pro Gly Asn				
	530	535		540
Gln Glu Lys Asp Pro Leu Leu Lys Asn Gln Glu Phe Lys Gly Val Ser				
545		550		555
				560

&lt;210&gt; 226

&lt;211&gt; 9

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 226

Ile Leu Ile Pro Ala Thr Trp Lys Ala

1

5

&lt;210&gt; 227

&lt;211&gt; 9



<212> PRT  
<213> Homo sapien

<400> 227  
Phe Leu Leu Asn Asp Asn Leu Thr Ala  
1 5

<210> 228  
<211> 9  
<212> PRT  
<213> Homo sapien

<400> 228  
Leu Leu Gly Asn Cys Leu Pro Thr Val  
1 5

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<211> 10  
<212> PRT  
<213> Homo sapien

<400> 229  
Lys Leu Leu Gly Asn Cys Leu Pro Thr Val  
1 5 10

<210> 230  
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<212> PRT  
<213> Homo sapien

<400> 230  
Arg Leu Thr Gly Gly Leu Lys Phe Phe Val  
1 5 10

<210> 231  
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<400> 231  
Ser Leu Gln Ala Leu Lys Val Thr Val  
1 5

<210> 232  
<211> 20  
<212> PRT  
<213> Homo sapiens

<400> 232  
Ala Gly Ala Asp Val Ile Lys Asn Asp Gly Ile Tyr Ser Arg Tyr Phe  
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Phe Ser Phe Ala  
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<210> 233

<211> 21

<212> PRT

<213> Homo sapiens

<400> 233

Phe Phe Ser Phe Ala Ala Asn Gly Arg Tyr Ser Leu Lys Val His Val  
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Asn His Ser Pro Ser  
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<210> 234

<211> 20

<212> PRT

<213> Homo sapiens

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Phe Leu Val Thr Trp Gln Ala Ser Gly Pro Pro Glu Ile Ile Leu Phe  
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Asp Pro Asp Gly  
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<210> 235

<211> 20

<212> PRT

<213> Homo sapiens

<400> 235

Leu Gln Ser Ala Val Ser Asn Ile Ala Gln Ala Pro Leu Phe Ile Pro  
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Pro Asn Ser Asp  
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<210> 236

<211> 20

<212> PRT

<213> Homo sapiens

<400> 236

Ile Gln Asp Asp Phe Asn Asn Ala Ile Leu Val Asn Thr Ser Lys Arg  
5 10 15

Asn Pro Gln Gln  
20

<210> 237

115

&lt;211&gt; 21

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 237

Arg Asn Ser Leu Gln Ser Ala Val Ser Asn Ile Ala Gln Ala Pro Leu  
5 10 15

Phe Ile Pro Pro Asn  
20

&lt;210&gt; 238

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 238

Thr His Glu Ser His Arg Ile Tyr Val Ala Ile Arg Ala Met Asp Arg  
5 10 15

Asn Ser Leu Gln  
20

&lt;210&gt; 239

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 239

Arg Asn Pro Gln Gln Ala Gly Ile Arg Glu Ile Phe Thr Phe Ser Pro  
5 10 15

Gln Ile Ser Thr  
20

&lt;210&gt; 240

&lt;211&gt; 21

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 240

Gly Gln Ala Thr Ser Tyr Glu Ile Arg Met Ser Lys Ser Leu Gln Asn  
5 10 15

Ile Gln Asp Asp Phe  
20

&lt;210&gt; 241

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 241

Glu Arg Lys Trp Gly Phe Ser Arg Val Ser Ser Gly Gly Ser Phe Ser  
5 10 15

Val Leu Gly Val  
20

&lt;210&gt; 242

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 242

Gly Ser His Ala Met Tyr Val Pro Gly Tyr Thr Ala Asn Gly Asn Ile  
5 10 15

Gln Met Asn Ala  
20

&lt;210&gt; 243

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 243

Val Asn His Ser Pro Ser Ile Ser Thr Pro Ala His Ser Ile Pro Gly  
5 10 15

Ser His Ala Met  
20

&lt;210&gt; 244

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 244

Ala Val Pro Pro Ala Thr Val Glu Ala Phe Val Glu Arg Asp Ser Leu  
5 10 15

His Phe Pro His  
20

&lt;210&gt; 245

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 245

Lys Pro Gly His Trp Thr Tyr Thr Leu Asn Asn Thr His His Ser Leu

117

5

10

15

Gln Ala Leu Lys  
20

<210> 246  
<211> 20  
<212> PRT  
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<400> 246  
Asn Leu Thr Phe Arg Thr Ala Ser Leu Trp Ile Pro Gly Thr Ala Lys  
5 10 15

Pro Gly His Trp  
20

<210> 247  
<211> 20  
<212> PRT  
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<400> 247  
Leu His Phe Pro His Pro Val Met Ile Tyr Ala Asn Val Lys Gln Gly  
5 10 15

Phe Tyr Pro Ile  
20

<210> 248  
<211> 20  
<212> PRT  
<213> Homo sapiens

<400> 248  
Pro Glu Thr Gly Asp Pro Val Thr Leu Arg Leu Leu Asp Asp Gly Ala  
5 10 15

Gly Ala Asp Val  
20

<210> 249  
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<213> Homo sapiens

<400> 249  
Gly Phe Tyr Pro Ile Leu Asn Ala Thr Val Thr Ala Thr Val Glu Pro  
5 10 15

Glu Thr Gly Asp

20

<210> 250  
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 <212> PRT  
 <213> Homo sapiens

<400> 250  
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Leu Thr Phe Arg  
                   20

<210> 251  
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<400> 251  
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                   5                  10                  15

Val Pro Pro Ala  
                   20

<210> 252  
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<400> 252  
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 Trp Arg Pro Val Lys Ala Ser Asp Gly Asp Tyr Tyr Thr Leu Ala Val  
                   20                  25                  30  
 Pro Met Gly Asp Val Pro Met Asp Gly Ile Ser Val Ala Asp Ile Gly  
           35                  40                  45  
 Ala Ala Val Ser Ser Ile Phe Asn Ser Pro Glu Glu Phe Leu Gly Lys  
   50                  55                  60  
 Ala Val Gly Leu Ser Ala Glu Ala Leu Thr Ile Gln Gln Tyr Ala Asp  
  65                  70                  75                  80  
 Val Leu Ser Lys Ala Leu Gly Lys Glu Val Arg Asp Ala Lys Ile Thr  
                   85                  90                  95  
 Pro Glu Ala Phe Glu Lys Leu Gly Phe Pro Ala Ala Lys Glu Ile Ala  
           100                  105                  110  
 Asn Met Cys Arg Phe Tyr Glu Met Lys Pro Asp Arg Asp Val Asn Leu  
           115                  120                  125  
 Thr His Gln Leu Asn Pro Lys Val Lys Ser Phe Ser Gln Phe Ile Ser  
  130                  135                  140  
 Glu Asn Gln Gly Ala Phe Lys Gly Met  
  145                  150

<210> 253  
 <211> 462  
 <212> DNA  
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<400> 253

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aagccagacc	gagatgtcaa	tctcaccac	caactaaatc	ccaaagtcaa	aagcttcagc	420
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<210> 254  
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 <212> DNA  
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<400> 254

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agacaaga	gagaatggaa	caaaattatt	ataatgaatt	ctgcagatat	ccatcacact	7860
ggcgccg	cgagcaccac	caccaccacc	actgagatcc	ggctgctaac	aaagcccgaa	7920
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&lt;210&gt; 255

&lt;211&gt; 401

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 255

gtggccagng actagaaggc gaggcgcgcg	gggaccatgg cggcggcggc	ggacgagcgg	60
agtccanagg acggagaaga cgaggaagag	gaggagcagt tggttctggt	ggaattatca	120
ggaattattg attcagactt cctctcaaaa	tgtgaaaata aatgcaaggt	tttgggcatt	180
gacactgaga ggcccattct gcaagtggac	agctgtgtct ttgctgggga	gtatgaagac	240
actctangga cctgtgttat atttgaagaa	aatgntnaac atgctgatac	agaaggcaat	300
aataaaacag tgctaaaata taaatgccat	acaatgaaga agctcagcat	gacaagaact	360
ctcctgacag agaagaagga aggagaagaa	aacatangtg g		401

<210> 256

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 256

tggtggncct gggatgggga accgcggtgg	cttccgngga ggtttcggca	ntggcatccg	60
gggcccgggt cgcgcccgng gacggggccg	gggccnangc cgngganctc	gcggangcaa	120
ggccgaggat aaggagtggg tgcccgtcac	caacttgggc cgcttgncca	aggacatgaa	180
nancaagccc ctgnaggaga tctatntctt	cttcctgcc ccattaagga	atcaagagat	240
catttgattt ctccctgggg gcctctctca	aggatnagggt ttttgaagat	tatgccagtg	300
canaaannan accccgttgc ccngtccatc	tncacccaac ncttccaagg	gcnatttttg	360
tttaggcctc attncngggg ggaaccttaa	cccaattttg g		401

<210> 257

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 257

atgtatgtaa aacattcat aaaatgtaaa	gggctataac aaatatgtta	taaagtgatt	60
ctctcagccc tgaggatatac agaatcattt	gcctcagact gctgttggtat	tttaaaattt	120
ttaaaatatac tgctaagtaa tttgctatgt	cttctccac actatcaata	tgctgtctc	180
taacaggctc ccactttct tttaatgtgc	tgttatgagc tttggacatg	agataaccgt	240
gcctgttcag agtgtctaca gtaagagctg	gacaaactct ggaggacac	agtctttgag	300
acagctcttt tggttgcttt ccactttct	gaaagggtta cagtaacctt	ctagataata	360
gaaactccca gttaaagcct angctancaa	tttttttttag t		401

<210> 258

<211> 401

<212> DNA

<213> Homo sapien

&lt;400&gt; 258

ggagcgctag gtcggtgtac gaccgagatt aggggtgcgtg ccagctccgg gaggccgcgg	60
tgagggggccg ggcccaagct gccgaccga gccgatcgtc agggtcgcca gcgcctcagc	120
tctgtggagg agcagcagta gtcggagggg gcaggatatt agaaatggct actccccagt	180
caattttcat ctttgcaatc tgcattttta tgataacaga attaattctg gcctcaaaaa	240
gctactatga tatcttaggt gtgccaaaat cggcatcaga gcgccaaatc aagaaggcct	300
ttcacaagtt ggccatgaag taccaccctg acaaaaataa gaccagatg ctgaagcaaa	360
attcagagag attgcagaag catatgaaac actctcagat g	401

&lt;210&gt; 259

&lt;211&gt; 401

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 259

attgggtttg gagggaggat gatgacagag gaatgccctt tggccatcac ggttttgatt	60
ctccagaata ttgtgggttt gatcatcaat gcagtcatgt taggctgcat tttcatgaaa	120
acagctcagg ctacagaag ggcagaaact ttgattttca gccgccatgc tgtgattgcc	180
gtccgaaatg gcaagctgtg cttcatgttc cgagtgggtg acctgaggaa aagcatgac	240
attagtgcct ctgtgcgcat ccaggtggtc aagaaaacaa ctacacctga aggggagggtg	300
gttcctattc accaactgga cattcctgtt gataacccaa tcgagagcaa taacattttt	360
ctggtggccc ctttgatcat ctgccacgtg attgacaagc g	401

&lt;210&gt; 260

&lt;211&gt; 363

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(363)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 260

aggaganang gaggggggana tgaataggga tggagaggga natagtggat gaggaggga	60
canggagagg aancagaaag gagaggcaag acaggagag acacancaca nangangana	120
caggtggggg ctgggggtggg gcatggagag ctttnangt cncaggcc accctgctct	180
cgctggngctg ttgaaaccca ctccatggct tcctgccact gcagttgggc ccagggtgg	240
cttattnctg gaatgcaagt ggctgtggct tggagcctcc cctctggnnn anggaaannn	300
attgctccct tatctgcttg gaatatctga gtttttccan cccggaaata aaacacacac	360
aca	363

&lt;210&gt; 261

&lt;211&gt; 401

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(401)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 261

cggtctccg ccgtctccc ggggtttcgg ggcacttggg tcccacagtc tggctctgct	60
tcacctccc ctgacctgag tagtcgccat ggcacagggt ctcagaggca ctgngactga	120

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cttccttgga tttgatgagc gggctgatgc anaaactctt cggaaggcta tgaaaggctt 180
gggcacagat gaggagagca tcctgaactc gttgacatcc cgaagtaatg ctcagcgcca 240
ggaaatctct gcagctttta agactctgtt tggcagggat cttctggatg acctgaaatc 300
agaactaact ggaaaatttg aaaaattaat tgtggctctg atgaaaccct ctcggcttta 360
tgatgcttat gaactgaaac atgccttgaa gggagctgga a 401

```

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<210> 262
<211> 401
<212> DNA
<213> Homo sapien

```

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<220>
<221> misc_feature
<222> (1) ... (401)
<223> n = A,T,C or G

```

```

<400> 262
agtctanaac atttctaata ttttgnngctt tcatatatca aaggagatta tgtgaaacta 60
tttttaataa ctgtaaagtg acatatagtt ataagatata tttctgtaca gtagagaaag 120
agtttataac atgaagaata ttgtaccatt atacattttc attctcgatc tcataagaaa 180
ttcaaaagaa taatgataga ggtgaaaata tgtttacttt ctctaaatca agcctagtgtg 240
tcaactcaaa aattatgntg catagtttta ttttgaattt aggttttggg actacttttt 300
tccancttca atgagaaaat aaaatctaca actcaggagt tactacagaa gttctaanta 360
tttttttgct aannagcnaa aaatataaac atatgaaaat g 401

```

```

<210> 263
<211> 401
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (401)
<223> n = A,T,C or G

```

```

<400> 263
ctgtccgacc aagagaggcc ggccgagccc gaggcttggg cttttgcttt ctggcggagg 60
gatctgcggc ggtttaggag gcggcgctga tcctgggagg aagaggcagc tacggcggcg 120
gcggcgggtg cggctagggc ggcggcgaat aaaggggccc cgcgcgggtg atgcggtgac 180
cactgcggca ggcccaggag ctgagtgggc cccggccctc agcccgtccc gncggacccg 240
ctttcctcaa ctctccatct tctcctgccg accgagatcg ccgaggcggn ctcaggctcc 300
ctanccctt ccccgteect tcccncccc cgtccccgcc ccgggggccc ccgccacccc 360
cctcccacca tggctctgaa ganaatccac aaggaattga a 401

```

```

<210> 264
<211> 401
<212> DNA
<213> Homo sapien

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<400> 264
aacaccagcc actccaggac ccctgaaggc ctctaccagg tcaccagtgt tctgcgccta 60
aagccacccc ctggcagaaa cttcagctgt gtgttctgga ataactcacgt gagggaaactt 120
actttggcca gcattgacct tcaaagtcag atggaaccca ggacccatcc aacttggtgtg 180
cttcacattt tcateccctc ctgcatcatt gctttcattt tcatagccac agtgatagcc 240
ctaagaaaac aactctgtca aaagctgtat tcttcaaaag acacaacaaa aagacctgtc 300

```

accacaacaa agaggggaagt gaacagtgct gtgaatctga acctgtggtc ttgggagcca 360  
gggtgacctg atatgacatc taaagaagct tctggactct g 401

<210> 265  
<211> 271  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(271)  
<223> n = A,T,C or G

<400> 265  
gccacttctt gtggacatgg gcagagcgct gctgccagtt cctggtagcc ttgaccacna 60  
cgctgggggg tctttgtgat ggtcatgggt ctcatttgca cttgggggtg tgggattcaa 120  
gttagaagtt tctagatctg gccgggcgca gtggctcaca cctgtaatcc cagcacttta 180  
ggaggctgag gcaggcggat catgagggtc ggagatcgag accgtcctgg ctaacacagt 240  
gaaaccccg tctactaaa aatacaaaaa a 271

<210> 266  
<211> 401  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(401)  
<223> n = A,T,C or G

<400> 266  
attcataaat ttagctgaaa gatactgatt caatttgtat acagngaata taaatgagac 60  
gacagcaaaa ttttcatgaa atgtaaaata tttttatagt ttgttcatac tatatgaggt 120  
tctattttta atgactttct ggatttttaa aaatttcttt aaatacaatc atttttgtaa 180  
tattttatatt atgcttatga tctagataat tgcagaatat cattttatct gactctgtct 240  
tcataagaga gctgtggccg aattttgaac atctgttata gggagtgatc aaattagaag 300  
gcaatgtgga aaaacaattc tgggaaagat ttctttatat gaagtccttg ccactagcca 360  
gccatcctaa ttgatgaaag ttatctgttc acaggcctgc a 401

<210> 267  
<211> 401  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(401)  
<223> n = A,T,C or G

<400> 267  
gaagaggcat cacctgatcc cggagacctt tggagttaag aggcggcgga agcgagggcc 60  
tgtggagtcg gatcctcttc ggggtgagcc agggtcggcg cgcgcggctg tctcanaact 120  
catgcagctg ttcccgcgag gcctgtttga ggacgcgctg ccgccatcg tgctgaggag 180  
ccaggtgtac agccttgtgc ctgacaggac cgtggccgac cggcagctga aggagcttca 240  
agagcanggg gagacaaaat cgtccagctg ggcttcnact tggatgccca tggaaanttat 300

tctttcnctt ganggactta cnngggaccc aagaancctt tncaaggggc ccttngtgga	360
tgggnccccga aaccccnnta tttgcccttg ggggggncca a	401

<210> 268  
 <211> 223  
 <212> DNA  
 <213> Homo sapien

<400> 268	
tgcgcatgtt ggccaggctg gtcttgaact cctgacttta agtgatccac ccgcctcaac	60
ctcccaaagt gctgggatta cagggtgtgag ccaccgcgcc tggcctgata catactttta	120
gaatcaagta gtcacgcact ttttctgttc atttttctaa aaagtaaata tacaaatgtt	180
ttgttttttg ttttttttgg ttgtttgttt ctgttttttt ttt	223

<210> 269  
 <211> 401  
 <212> DNA  
 <213> Homo sapien

<400> 269	
actatgtaaa ccacattgta cttttttttta ctttggcaac aaatatttat acatacaaga	60
tgctagtcca tttgaatatt tctcccaact tatccaagga tctccagctc taacaaaatg	120
gtttattttt atttaaagt caatagttgt tttttaaaat ccaaatacaga ggtgcaggcc	180
accagttaaa tgccgtctat cagggtttgt gccttaagag actacagagt caaagctcat	240
ttttaaagga gtaggacaaa gttgtcacag gtttttggtg ttgtttttat tgcccccaa	300
attacatgtt aatttccatt tatatcaggg attctattta ctgaagact gtgaagttgc	360
cattttgtct cattgttttc tttgacataa ctaggatcca t	401

<210> 270  
 <211> 401  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (401)  
 <223> n = A,T,C or G

<400> 270	
tggtgttga ttcacctcag cactgcttgg tatctgcacc ctacctctct ttagaggctg	60
ccttgtcaac tgaaaaatgc acctgacttc gagcaagact ctttccttag gttctggatc	120
tgtttgagcc ccatggcact gagctggaat ctgagggctc tgttccaagg atgtgatgat	180
gtgggagaat gttctttgaa agagcagaaa tccagtctgc atggaaacag cctgtagagn	240
agaagtttcc agtgataagt gttcactgtt ctaaggagggt acaccacagc tacctgaatt	300
ttcccaaaat gagtgttct gtgcgttaca actggccttt gtacttgact gtgatgactt	360
tgttttttct tttcaattct anatgaacat gggaaaaaat g	401

<210> 271  
 <211> 329  
 <212> DNA  
 <213> Homo sapien

<400> 271	
ccacagcctc caagtcagggt ggggtggagt ccagagctg cacagggttt ggcccaagtt	60
tctaagggag gcacttcttc ccttcgcca tcaagtccag cccctgctgg ctggtgctg	120

```

agccccctcag acagccccct gccccgcagg cctgccttct cagggacttc tgcggggcct      180
gaggcaagcc atggagttag acccaggagc cggacacttc tcaggaaatg gcttttccca      240
acccccagcc cccaccgggt ggttcttcct gttctgtgac tgtgtatagt gccaccacag      300
cttatggcat ctcataggag acaaaaaaa                                329

```

```

<210> 272
<211> 401
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(401)
<223> n = A,T,C or G

```

```

<400> 272
nggctgntaa cntcggagggt nacttcctgg actatcctgg agacccccctc cgcttccacg      60
nncatnatat cntcatngc tgggcccntn angacacnat cccactccaa cacctgngng      120
atgctggncn cctnggaacc anentcagaa ngaccctgnt cntntgtntt ccgcaanctg      180
aagnnaangc gggntacacc tnentgcant ggnccacnct gcngggaact ntacacacct      240
acgggatgtg gctgcgccaan gagccaagag cntttctgga tgattcccca gcctcttgnn      300
agggantcta caacattgct nnntaccttt ntcenncngc nnntnntgga ntacaggngn      360
tnntaact acatcttttt tactgcncn tncttgggtg g                                401

```

```

<210> 273
<211> 401
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(401)
<223> n = A,T,C or G

```

```

<400> 273
cagcaccatg aagatcaaga tcatcgacc cccagagcgc aagtactcgg tgtggatcgg      60
tggctccatc ctggcctcac tgtccacctt ccagcagatg tggattagca agcaggagta      120
cgacgagtcg ggccccctcca tegtccaccg caaatgcttc taaacggact cagcagatgc      180
gtagcatttg ctgcatgggt taattgagaa tagaaatttg cccctggcaa atgcacacac      240
ctcatgctag cctcacgaaa ctggaataag ccttcgaaaa gaaattgtcc ttgaagcttg      300
tatctgatat cagcactgga ttgtagaact tgttgctgat tttgaccttg tattgaagtt      360
aactgttccc cttggtatta acgtgtcagg gctgagtnt c                                401

```

```

<210> 274
<211> 401
<212> DNA
<213> Homo sapien

```

```

<400> 274
ccaccacac ccaccgcgcc ctcttctcgg gagccagtcc gcgccaccgc      60
cgccgccag gccatcgcca cctccgcag ccatgtccac caggtcctg tctctgtcct      120
cctaccgcag gatgttcggc ggccgggca ccgcgagccg gccgagctcc agccggagct      180
acgtgactac gtccaccgc acctacagcc tgggcagcgc gctgcgccc agcaccagcc      240
gcagcctcta cgctcgtcc ccggggcggc tgtatgccac gcgtcctct gccgtgcgcc      300
tgcggagcag cgtgcccggg gtgcggctcc tgcaggactc ggtggacttc tcgctggccg      360

```

acgccatcaa caccgagttc aagaacaccc gcaccaacga g 401

<210> 275  
 <211> 401  
 <212> DNA  
 <213> Homo sapien

<400> 275  
 ccacttccac cactttgtgg agcagtgcct tcagcgcaac cgggatgcc a ggtatccctg 60  
 ctggcctggg cctgggcttc gggagagcag aggggtgctca ggagggt aag gccagggtgt 120  
 gaagggaactt acctcccaa ggttctgcag gggaatctgg agctacacac aggagggatc 180  
 agtccttggg tgtgtcagag gccagcctgg ggagctctgg ccaactgcttc ccatgagctg 240  
 agggagaggg agaggggacc cgaggctgag gcataagtgg caggatttcg ggaagctggg 300  
 gacacggcag tgatgctgcg gtctctcttc ccctttccct ccaggcccag tgccagcacc 360  
 ctctgaacc actctttctt caagcagatc aagcgacgtg c 401

<210> 276  
 <211> 401  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)... (401)  
 <223> n = A,T,C or G

<400> 276  
 tctgatattg ntacccttga gccacctaag ttagaagaaa ttggaaatca agaagttgtc 60  
 attggtgaag aagcacagag ttcagaagac tttaacatgg gctcttcttc tagcagccag 120  
 tatactttct gtcagccaga aactgtattt tcattctcagc ctagtgatga tgaatcaagt 180  
 agtgatgaaa ccagtaatca gccagtcctt gccttttagac gacgcccgtgc taggaagaag 240  
 accgtttctg cttcagaatc tgaagaccgg ctagtgtggg aacaagaaac tgaaccttct 300  
 aaggagttga gtaaagctca gttcagtagt ggtctcaata agtgtgttat acttgctttg 360  
 tgattgcaa tcagcatggg atttggccat ttctatggca c 401

<210> 277  
 <211> 401  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)... (401)  
 <223> n = A,T,C or G

<400> 277  
 aactttggca acatatctca gcaaaaacta cagctatggt attcatgcc a aaataaaagc 60  
 tgtgcagagg agtggctgca atgaggtcac aacggtgggt gatgtaaaag agatcttcaa 120  
 gtcctcatca cccatccctc gaactcaagt cccgctcatt acaaattctt cttgccagtg 180  
 tccacacatc ctgccccatc aagatgttct catcatgtgt tacgagnggc gctcaaggat 240  
 gatgcttctt gaaaattgct tagttgaaaa atggagagat cagcttagta aaagatccat 300  
 acagtgggaa gagaggctgc aggaacagcg ganaacagtt caggacaaga agaaaacagc 360  
 cgggcgcacc agtcgtagta atcccccaa accaaaggga a 401

<210> 278



<211> 401  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(401)  
 <223> n = A,T,C or G

<400> 278  
 aatgagtgtg agaccacaaa tgaatgccgg gaggatgaaa tgtgttggaa ttatcatggc 60  
 ggcttccgtt gttatccacg aaatccttgt caagatccct acattctaac accagagAAC 120  
 cgatgtgttt gccagtcctc aaatgccatg tgccgagAAC tgcccagtc aatagtctac 180  
 aaatacatga gcatccgATC tgataggTCT gtgccatcag acatcttcca gatacaggcc 240  
 acaactatTT atgccaacac catcaatact tttcggatta aatctggaaa tgaaaatgga 300  
 gagtctacCT acgacaacaa anccctgtaa gtgcaatgct tgtgctcgtg aagncattat 360  
 caggaccaag agaacatatc gtggacctgg agatgctgac a 401

<210> 279  
 <211> 401  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(401)  
 <223> n = A,T,C or G

<400> 279  
 aaattattgc ctctgataca tacctaagtn aacanaacat taatacctaa gtaaACATAA 60  
 cattaCTTgg aggggttgCag nttctaantg aaactgtatt tgaaactttt aagtataCTT 120  
 taggaaacaa gcatgaacgg cagtctagaa taccagaaac atctactTgg gtagcttggN 180  
 gccattatcc tgtggaatct gatatgtctg gnagcatgtc attgatggga catgaagaca 240  
 tctttggaaa tgatgagatt atttcctgtg ttaaaaaaaaa aaaaaatctt aaattcctac 300  
 aatgtgaaac tgaaactaat aattttgatc ctgatgtatg ggacagcgta tctgtaccag 360  
 gctctaaata acaaaaagnta gggngacaag nacatgttcc t 401

<210> 280  
 <211> 326  
 <212> DNA  
 <213> Homo sapien

<400> 280  
 gaagtggAAT tgtataattc aattcgataa ttgatctcat gggctttccc tggaggaaag 60  
 gttttttttg ttgttttttt tttAagaact tgaaacttgt aaactgagat gtctgtagct 120  
 tttttgcca tctgtagtgt atgtgaagat ttcaaaacct gagagcactt tttctttgtt 180  
 tagaattatg agaaaggcac tagatgactt taggatttgc atttttccct ttattgcctc 240  
 atttcttgtg acgccttgtt ggggagggaa atctgtttat tttttcctac aaataaaaag 300  
 ctaagattct atatcgcaaa aaaaaa 326

<210> 281  
 <211> 374  
 <212> DNA  
 <213> Homo sapien

<400> 281  
caacgcgttt gcaaatatc ccctggtagc ctacttcctt acccccgaat attggtaaga 60  
tcgagcaatg gcttcaggac atgggttctc ttctcctgtg atcattcaag tgctcactgc 120  
atgaagactg gcttgtctca gtgtttcaac ctcaccaggg ctgtctcttg gtccacacct 180  
cgctccctgt tagtgccgta tgacagcccc catcaaataga ccttggccaa gtcacgggtt 240  
ctctgtggtc aagggttggtt ggctgattgg tggaaagtag ggtggaccaa aggaggccac 300  
gtgagcagtc agcaccagtt ctgcaccagc agcgccctccg tcctagtggg tgttcctgtt 360  
tctcctggcc ctgg 374

<210> 282  
<211> 404  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1) ... (404)  
<223> n = A,T,C or G

<400> 282  
agtgtggtgg aattcccga tcctannccg cgactcacac aaggcagagt ngccatggag 60  
aaaattccag tgtcagcatt cttgtctcct gtggccctct cctacactct ggccagagat 120  
accacagtca aacctgnagc caaaaaggac acaaaggact ctgcacccaa actgccccan 180  
accctctcca gaggttgggg tgaccaactc atctggactc anacatatga agaagctcta 240  
tataaatcca agacaagcaa caaaccttg atgattattc atcacttgga tgagtgecca 300  
cacagtcaag ctttaaagaa agtgtttgct gaaaataaag aaatccagaa attggcagag 360  
cagtttgtcc tcctcaatct ggtttatgaa acaactgaca aaca 404

<210> 283  
<211> 184  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1) ... (184)  
<223> n = A,T,C or G

<400> 283  
agtgtggtgg aattcacttg cttaanttgt gggcaaaaga gaaaaagaag gattgatcag 60  
agcattgtgc aatacagttt cattaactcc ttccctcgct cccccaaaaa tttgaatttt 120  
tttttcaaca ctcttacacc tgttatggaa aatgtcaacc tttgtaagaa aaccaaaata 180  
aaaa 184

<210> 284  
<211> 421  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1) ... (421)  
<223> n = A,T,C or G

<400> 284

```

ctattaatcc tgccacaata tttttaatta cgtacaaaga tctgacatgt caccagggga      60
cccatttcac ccactgctct gtttggecgc cagtcttttg tctctctctt cagcaatggg      120
gaggcggata ccctttcttc ggggaanana aatccatggg ttgttgccct tgccaataac      180
aaaaatggtg gaaagtcgag tggcaaagct gttgccattg gcattcttca cgtgaaccac      240
gtcaaaagat ccagggtgcc tctctctgtt ggtgatcaca ccaattcttc ctagggttagc      300
acctccagtc accatacaca ggttaccagt gtogaacttg atgaaatcag taatcttgcc      360
agtctctaaa tcaatctgaa tggatatcatt caccttgatg aggggatcgg ggtagcggat      420
g                                                                    421

```

<210> 285

<211> 361

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(361)

<223> n = A,T,C or G

<400> 285

```

ctgggtggta actctttatt tcattgtccg gaanaaagat gggagtggga acagggtgga      60
cactgtgcag gcttcagctt ccactccggg caggattcag gctatctggg accgcaggga      120
ctgccagggt cacagccctg gctcccaggg caggcaggga aggtgacggg actggaagcc      180
ctttcanag ccttgaggga gctgggtccg ccacaagcaa tgagtgccac tctgcagttt      240
gcaggggatg gataaacagg gaaacactgt gcattcctca cagccaacag tgtaggtctt      300
ggtgaagccc cggcgctgag ctaagctcag gctgttccag ggagccacga aactgcaggt      360
a                                                                    361

```

<210> 286

<211> 336

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(336)

<223> n = A,T,C or G

<400> 286

```

tttgagtggc agcgccttta tttgtggggg ccttcaagggn agggctcgtg ggggcagcgg      60
ggaggaanag ccganaaaact gtgtgaccgg ggccctcagg ggtgggcatt gggggctcct      120
cttgcanatg ccatttgcca tcaccgggtg agccattggg ggcagcgggt accggtcctt      180
tcttgttcaa catagggtag gtggcagcca cgggtccaac tcgcttgagg ctgggccctg      240
ggcgctccat tttgtgttcc angagcatgt ggttctgtgg cgggagcccc acgcaggccc      300
tgaggatgtt ctcatgacag ctgcgctggc ggaaaaa                        336

```

<210> 287

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 287  
 tgggtaccaaa atttntttat ttgaaggaat ggnacaaatc aaanaactta agnggatgtt 60  
 ttggtacaac ttatanaaaa ggnaaaggaa accccaacat gcatgcnctg ccttgngnac 120  
 caggggaagtc accccaacggc tatgggggaaa ttanccccgag gcttancttt cattatcact 180  
 gtctcccagg gngngcttgt caaaaanata ttccnccaag ccaaattcgg gcgctcccat 240  
 nttgcncaag ttggtcacgt ggtcacccaa ttctttgatg gctttcacct gctcattcag 300  
 g 301

<210> 288  
 <211> 358  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(358)  
 <223> n = A,T,C or G

<400> 288  
 aagtttttaa acttttttatt tgcataattaa aaaaattgng cattccaata attaaaaatca 60  
 tttgaacaaa aaaaaaatg gcactctgat taaactgcat tacagcctgc aggacacctt 120  
 gggccagctt ggttttactc tanatttcac tgctgtccca cccacttct tccacccac 180  
 ttcttccttc accaacatgc aagttctttc ctccctgcc agccanata tagacagat 240  
 gggaaaggca ggcgcggcct tcgttgctcag tagttctttg atgtgaaagg ggcagcacag 300  
 tcatttaaac ttgatccaac ctctttgcat cttacaaagt taaacagcta aaagaagt 358

<210> 289  
 <211> 462  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(462)  
 <223> n = A,T,C or G

<400> 289  
 ggcatcagaa atgctgttta tttctctgct gctcccaagc tggctggcct ttgcagagga 60  
 gcagacaaca gatgcatagt tgggganaaa gggaggacag gttccaggat agaggggtgca 120  
 ggctgagga ggaagggtaa naggaaggaa ggccatcctg gatccccaca tttcagtctc 180  
 anatgaggac aaagggactc ccaagcccc aaatcatcan aaaacaccaa ggagcaggag 240  
 gagcttgagc aggccccagg gagcctcana gccataaccag ccactgtcta ctcccatcc 300  
 tcctctccca ttccctgtct gttcanacc acctccagc taagccccag ctccattccc 360  
 ccaatcctgg cccttgccag cttgacagtc acagtgcctg gaattccacc actgaggctt 420  
 ctcccagttg gattaggacg tcgcctgtt agcatgctgc cc 462

<210> 290  
 <211> 481  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(481)

<223> n = A,T,C or G

<400> 290

tactttccta	aactttatta	aagaaaaaag	caataagcaa	tgngngtaaa	tctctanaac	60
ataccecaatt	ttctgggctt	cctccccoga	gaatgtgaca	ttttgatttc	caaacatgcc	120
anaagtgtat	ggttcccaac	tgtactaaag	taggtganaa	gctgaagtcc	tcaagtgttc	180
atcttccaac	ttttcccagt	ctgtggtctg	tctttggatc	agcaataatt	gcctgaacag	240
ctactatggc	ttcgttgatt	tttgtctgta	gctctctgag	ctcctctatg	tgacagcaatc	300
gcanaatttg	agcagcttca	ttaanaactg	catctcctgt	gtcaaaaacca	anaatatgtt	360
tgtctaaagc	aacaggtaag	ccctcttttg	tttgatttgc	cttancaact	gcctcctgtg	420
tcaggcgctc	ctgaaccaa	atccgaattg	ccttaagcat	taccaggtaa	tcctcatgac	480
g						81

<210> 291

<211> 381

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(381)

<223> n = A,T,C or G

<400> 291

tcataagtaat	gtaaaaccat	ttgtttaatt	ctaaatcaaa	tcactttcac	aacagtgaag	60
attagtact	ggtaagng	tgccactgta	catatcatca	ttttctgact	ggggtcagga	120
cctggctcta	gtccacaagg	gtggcaggag	gagggtggag	gctaanaaca	cagaaaacac	180
acaaaanaaa	ggaaagctgc	cttgccanaa	ggatgaggng	gtgagcttgc	cgaaggatgg	240
tggaagggg	gctccctgtt	ggggccgagc	caggagtccc	aagtcagctc	tcctgcctta	300
cttagctcct	ggcanagggt	gagtggggac	ctacgaggtt	caaaatcaaa	tggcatttgg	360
ccagcctggc	tttactaaca	g				381

<210> 292

<211> 371

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(371)

<223> n = A,T,C or G

<400> 292

gaaaaaataa	tcgtttta	tgaaaaac	gnaggatact	attccactcc	cccanatgag	60
gaggctgagg	anaccaaacc	cctacatcac	ctcgtagcca	cttctgatac	ttttcacgag	120
gcagcaggca	aagacaattc	ccaaaacctc	nacaaaagca	attccaaggg	ctgctgcagc	180
taccaccanc	acattttttc	tcagccagcc	cccaatcttc	tcacacagc	cctccttatg	240
gategccttc	tcgttgaaat	taatccaca	gccacagta	acattaatgc	ancaggagtc	300
ggggactcgg	ttcttcgaca	tggaagggat	tttctcccaa	tctgtgtagt	tagcagcccc	360
acagcactta	a					371

<210> 293

<211> 361

<212> DNA

<213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(361)  
 <223> n = A,T,C or G

<400> 293  
 gattttaaag aaaacacttt attgttcagc aattaaaagt tagccaaata tgtatttttc 60  
 tccataattt attgngatgt tatcaacatc aagtaaaatg ctcattttca tcatttgctt 120  
 ctgttcatgt tttcttgaac acgtcttcaa ttttccttcc aaaatgctgc atgccacact 180  
 tgaggtaacg aagcanaagt atttttaaac atgacagcta anaacattca tctacagcaa 240  
 cctatatgct caatacatgc cgcgtgatcc tagtagtttt ttcacaacct tctacaagtt 300  
 tttggaaaac atctgttatg atgactttca tacaccttca cctcaaaggc tttcttgcac 360  
 c 361

<210> 294  
 <211> 391  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(391)  
 <223> n = A,T,C or G

<400> 294  
 tattttaaag tttaattatg attcanaaaa aatcgagcga ataactttct ctgaaaaaat 60  
 atattgactc tgtatanacc acagttattg gggganaagg gctggtagg taaattatcc 120  
 tattttttat tctgaaaatg atattaatan aaagtcctcg ttcagctctg attataaaga 180  
 tacatatgcc caaaatggct ganaataaat acaacaggaa atgcaaaagc tgtaaagcta 240  
 agggcatgca ananaaaatc tcanaatacc caaagnggca acaaggaacg tttggctgga 300  
 atttgaagtt atttcagtca tctttgtctt tggctccatg tttcaggatg cgtgtgaact 360  
 c gatgtaatt gaaattcccc tttttatcaa t 391

<210> 295  
 <211> 343  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(343)  
 <223> n = A,T,C or G

<400> 295  
 ttcttttggt ttattgataa cagaaactgt gcataattac agatttgatg aggaatctgc 60  
 aaataataaa gaatgtgtct actgccagca aaatacaatt attccatgcc ctctcaacat 120  
 acaaatatag agttcttcac accanatggc tctggtgtaa caaagccatt ttanatgttt 180  
 aattgtgctt ctacaaaacc ttcanagcat gaggtagttt cttttaccta cnatattttc 240  
 cacattttca ttattacact tttagtgage taaaatcett ttaacatagc ctgcggatga 300  
 tctttcacaa aagccaagcc tcatttaca agggtttatt tct 343

<210> 296  
 <211> 241  
 <212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (241)

<223> n = A,T,C or G

<400> 296

ttcttgata ttggttgttt ttgtgaaaaa gtttttgttt ttcttctcag tcaactgaat	60
tatttctcta ctttgccctc ctgatgccca catgananaa cttaanataa tttctaacag	120
cttcactttt ggaaaaaaaa aaacacctgtt ttcctcatgg aacccagga gttgaaagtg	180
gatanatcgc tctcaaatc taaggctctg ttcagcttta cattatgta cctgacgttt	240
t	241

<210> 297

<211> 391

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (391)

<223> n = A,T,C or G

<400> 297

gttgtggctg anaatgctgg agatgctcag ttctctccct cacaaggtag gccacaaatt	60
cttggtgggtg ccctcacatc tggggtcttc aggcaccagc catgcctgcc gaggagtgt	120
gtcaggacan accatgtccg tgctaggccc aggcacagcc caaccactcc tcatccaagt	180
ctctcccagg tttctggtcc cgatgggcaa ggatgacccc tccagtggct ggtacccac	240
cateccacta cccctcacat gctctcactc tccatcaggt cccaatcct ggcttccctc	300
ttcacgaact ctcaaagaaa aggaaggata aaacctaaat aaaccagaca gaagcagctc	360
tggaaaagta caaaaagaca gccagaggtg t	391

<210> 298

<211> 321

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (321)

<223> n = A,T,C or G

<400> 298

caagccaaac tgtntccagc tttattaaan ataactttcca taaacaatca tggatatttca	60
ggcaggacat gggcanacaa tcgttaacag tataacaaca ctttcaaact cccttnttca	120
atggactacc aaaaatcaaa aagccactat aaaacccaat gaagtcttca tctgatgtc	180
tgaacaggga aagttttaaag ngagggttga catttcacat ttagcatgtt gtttaacaac	240
ttttcacaag ccgacctga ctttcaggaa gtgaaatgaa aatggcanaa tttatctgaa	300
natccacaat ctaaaaatgg a	321

<210> 299

<211> 401

<212> DNA

<213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(401)  
 <223> n = A,T,C or G

<400> 299  
 tatcataaag agtgttgaag tttatatttatt atagcaccat tgagacattt tgaaattgga 60  
 attggtaaaa aaataaaaaca aaaagcattt gaattgtatt tggnggaaca gcaaaaaaag 120  
 agaagtatca tttttctttg tcaaattata ctgtttccaa acatttttga aataaataac 180  
 tggaattttg tcggtcactt gcaactgggtg acaagattag aacaagagga acacatatgg 240  
 agttaaatTT tttttgttgg gatttcanat agagtttggg ttataaaaag caaacagggc 300  
 caacgtccac accaaaattct tgatcaggac caccaatgtc atagggngca atatctacaa 360  
 taggtagtct cacagccttg cgtgttcgat attcaaagac t 401

<210> 300  
 <211> 188  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(188)  
 <223> n = A,T,C or G

<400> 300  
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 ggtgtatctt gttttctaata agataaaactt ttttgtcttt gctttatctt attagggagt 120  
 tgtatgtcag tgtataaaac atactgtgtg gtataacagg cttaataaat tctttaaaag 180  
 gaaaaaaa 188

<210> 301  
 <211> 291  
 <212> DNA  
 <213> Homo sapien

<400> 301  
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 acactaaaga aatcctctgt gcttttcaat atgcaaatat atttcttcca agagttgccc 120  
 tgggtgtgact tcaagagttc atgttaactt cttttctgga aacttccttt tcttagttgt 180  
 tgtattcttg aagagcctgg gccatgaaga gcttgcttaa gttttgggca gtgaactcct 240  
 tgatgttctg gcagtaagtg tttatctggc ctgcaatgag cagcgagtcc a 291

<210> 302  
 <211> 341  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(341)  
 <223> n = A,T,C or G

<400> 302  
 tgatttttca taattttatt aaatnatcac tgggaaaact aatggttcgc gtatcacaca 60



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attacactac aatctgatag gagtggtaaa accagccaat ggaatccagg taaagtacaa      120
aaacgccacc ttttattgtc ctgtcttatt tctcggaag gaggggtcta ctttacacat      180
ttcatgagcc agcagtggac ttgagttaca atgtgtaggt tccttggtgt tatagctgca      240
gaagaagcca tcaaattctt gaggacttga catctctcgg aaagaagcaa actagtggat      300
ccccggggtc gcaggaattc gatatcaagc ttatcgatac c                          341

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<210> 303

<211> 361

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(361)

<223> n = A,T,C or G

<400> 303

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tgcagacagt aaatnaattt tatttgngtt cacagaacat actaggcgat ctcgacagtc      60
gctccgtgac agcccaccaa cccccaaccc tntacctcgc agccacccta aaggcgactt      120
caanaanatg gaaggatctc acggatctca ttctaattgg tccgccgaag tctcacacag      180
tanacagacg gaggttganat gctggaggat gcagtcacct cctaaactta cgaccaccca      240
ccanacttca tcccagccgg gacgtcctcc cccacccgag tcctcccatc ttcttctcct      300
actttgccgc agttccaggn gtcctgcttc caccagtccc acaaagctca ataaatacca      360
a

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<210> 304

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 304

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tagctccgcc cgccaggctc tgtgccgcct ccccgaggc gcanattcat gaacacgggtg      120
ctcagggggt tgaggccgta ctccccagc gggagctggt cctccagggg ctccccctcg      180
aaggtcagcc anaacaggtc gtctgcaca cctccagcc cgtcacttg ctgcttcagg      240
tgggccacgg tctgcgtcag ccgcacctcg taggtgctgc tgcggccctt gttattctc      300
a

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<210> 305

<211> 331

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(331)

<223> n = A,T,C or G

<400> 305

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tcgacgttct	cctccttggc	actggccaag	gtctcttcta	ggcatcgat	ggttttctcc	180
aactttgcca	canacctctc	ggcaaaactct	gctcgggtct	cancctcctt	cagcttctcc	240
tccaacagtt	tgatctcctc	ttcatattta	tcttctttgg	gggaatactc	ctcctctgag	300
gccatcaggg	acttgagggc	ctggtccatg	g			331

<210> 306  
 <211> 457  
 <212> DNA  
 <213> Homo sapien

<400> 306						
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aattatatgt	atcaaatata	taagtaaaaa	aaagtttagac	tttcaagcct	gtaatccag	180
cactttggga	ggctgaggca	ggtggatcac	taacattaaa	aagacaacat	tagattttgt	240
cgatttatag	caattttata	aatatataac	tttgtcactt	ggatcctgaa	gcaaaataat	300
aaagtgaatt	tgggattttt	gtacttggtg	aaaagtttaa	caccctaaat	tcacaactag	360
tggatccccc	gggctgcagg	aattcgatat	caagcttata	gataccgtcg	acctcgaggg	420
ggggcccggg	acccaattcg	ccctatagtg	agtcgta			457

<210> 307  
 <211> 491  
 <212> DNA  
 <213> Homo sapien

<400> 307						
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gcgcagccac	cgccgcgcgc	gccgcctctc	cttagtcgcc	gccatgacga	ccgcgtccac	180
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cctggagctc	tacgcctcct	acgtttacct	gtccatgtct	tactactttg	accgcgatga	300
tgtggctttg	aagaactttg	ccaaataactt	tcttcaccaa	tctcatgagg	agaggggaaca	360
tgtgagaaa	ctgatgaagc	tgcagaacca	acgaggtggc	cgaatcttcc	ttcaggatat	420
caagaaacca	gactgtgatg	actgggagag	cgggctgaat	gcaatggagt	gtgcattaca	480
tttggaaaaa	a					491

<210> 308  
 <211> 421  
 <212> DNA  
 <213> Homo sapien

<400> 308						
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aggccctgga	tgtgatgggt	tccaccttcc	acaagtactc	gggcaaagag	ggtgacaagt	120
tcaagctcaa	caagtcagaa	ctaaaggagc	tgctgaccgc	ggagctgccc	agcttcttgg	180
ggaaaaggac	agatgaagct	gctttccaga	agctgatgag	caacttgga	agcaacaggg	240
acaacgaggt	ggacttccaa	gagtactgtg	tcttctgtc	ctgcatcgcc	atgatgtgta	300
acgaattctt	tgaaggcttc	ccagataagc	agcccaggaa	gaaatgaaaa	ctcctctgat	360
gtggttgggg	ggtctgccag	ctggggccct	ccctgtcgcc	agtgggcact	tttttttttc	420
c						421

<210> 309  
 <211> 321  
 <212> DNA

<213> Homo sapien

<400> 309

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tggggaaccg	cgggtggcttc	cgcggagggt	tcggcagtg	catccggggc	cggggtcgcg	120
gccgtggacg	gggcccgggc	cgaggccgcg	gagctcgcg	aggcaaggcc	gaggataagg	180
agtggatgcc	cgtcaccaag	ttgggcccgt	tggtcaagga	catgaagatc	aagtccttgg	240
aggagatcta	tctcttctcc	ctgcccatta	aggaatcaga	gatcattgat	ttcttcttgg	300
gggcctctct	caaggatgag	g				321

<210> 310

<211> 381

<212> DNA

<213> Homo sapien

<400> 310

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tcagtgccta	tttttcttgg	aaactcaatt	ttaaatagtc	caattccatc	tgaagccaag	120
ctgttgtcat	tttcattcgg	tgacattctc	tcccatgaca	cccagaagg	gcagaagaac	180
cacatttttc	atttatagat	gtttgcatcc	tttgtattaa	aattattttg	aaggggttgc	240
ctcattggat	ggcttttttt	tttttctctc	agggagaagg	ggagaaatgt	acttggaat	300
taatgtatgt	ttacatctct	ttgcaaattc	ctgtacatag	agatatattt	tttaagtgtg	360
aatgtaacaa	catactgtga	a				381

<210> 311

<211> 538

<212> DNA

<213> Homo sapien

<400> 311

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cataccacaa	gagaagttaa	tttcttaaca	ttgtgttcta	tgattatttg	taagaccttc	120
accaagtctt	gatattcttt	aaagacatag	ttcaaaattg	cttttgaaaa	tctgtattct	180
tgaaaatata	cttgtttgtg	attagggttt	taaataaccag	ctaaaggatt	acctcactga	240
gtcatcagta	ccctcctatt	cagctcccca	agatgatgtg	tttttgctta	ccctaagaga	300
ggttttcttc	ttatttttag	ataattcaag	tgcttagata	aattatgttt	tctttaagtg	360
tttatggtaa	actcttttaa	agaaaattta	atatgttata	gctgaatctt	tttggttaact	420
ttaaatcttt	atcatagact	ctgtacatat	gttcaaatta	gctgcttgcc	tgatgtgtgt	480
atcatcggtg	ggatgacaga	acaaacatat	ttatgatcat	gaataatgtg	ctttgtaa	538

<210> 312

<211> 176

<212> DNA

<213> Homo sapien

<400> 312

ggaggagcag	ctgagagata	gggtcagtga	atgcggttca	gcctgctacc	tctcctgtct	60
tcatagaacc	attgccttag	aattattgta	tgacacgttt	tttggttggt	aagctgtaag	120
gttttgttct	ttgtgaacat	gggtattttg	aggggagggg	ggagggagta	gggaag	176

<210> 313

<211> 396

<212> DNA

<213> Homo sapien

&lt;400&gt; 313

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tggcgct	ccc	atggctct	tg	caacat	ctcc	ccttcg	tttt	tgagggg	gtc	atgccg	gggg	120
agccacc	agc	ccctcact	gg	gttcgg	agga	gagtcag	gaa	gggcca	agca	cgacaa	agca	180
gaaacat	cgg	atttgggg	aa	cgcgtg	tcaa	tccctt	gtgc	cgcaggg	cgtg	ggcggg	agag	240
actgtt	ctgt	tcctt	gtgt	actgt	gttg	tgaaag	acta	cctcg	ttct	gtctt	gatgt	300
gtcacc	gggg	caactg	cctg	ggggc	gggg	tggggg	cagg	gtgga	agcg	ctcccc	at	360
tatacca	aaag	gtgctac	atc	tatgt	gatg	gtggg						396

&lt;210&gt; 314

&lt;211&gt; 311

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 314

cctcaac	atc	ctcagag	agg	actgga	agcc	agtcct	tacg	ataaa	actcca	taattt	atgg	60	
cctgcag	tat	ctctt	cttg	agccca	accc	cgagg	accca	ctgaac	aaagg	aggccg	caga	120	
ggcctg	cag	aacaac	cggc	ggctg	tttg	gcaga	acgtg	cagcg	ctcca	tgccgg	gtgg	180	
ctacat	cggc	tccac	tact	ttgag	cgtg	cctgaa	atag	ggttg	ggcg	ca	taccc	acccc	240
cgccac	ggcc	acaag	ccctg	gcatc	ccctg	caaata	ttta	ttggg	gggcca	tggtg	taggg	300	
tttggg	gggg	gc										311	

&lt;210&gt; 315

&lt;211&gt; 336

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 315

tttaga	acat	ggttat	catc	caagact	tact	ctacc	ctgca	acattg	aact	cccaag	agca	60
aatccac	att	cctctt	gagt	tctgc	agctt	ctgtg	ttaa	agggc	agctg	tcgtc	tatgc	120
cgtaga	aatca	catgat	ctga	ggacc	attca	tgga	agctg	taaat	agcct	agtc	tgggga	180
gtctt	ccata	aagttt	tgc	tggag	caa	aac	caggatt	aaact	aggtt	tgg	ttccttc	240
agccct	ctaa	aagcat	aggg	cttag	cctgc	aggct	tcctt	ggg	ctttctc	tgtgt	gtgtga	300
gtttt	gtaaa	cactat	agca	tctgt	ttaaga	tccagt						336

&lt;210&gt; 316

&lt;211&gt; 436

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 316

aacatg	gtct	gcgtgc	ctta	agagag	acgc	ttcctg	caga	acagg	ac	actac	aaaga	60
atgttt	ccat	tggaat	tgtt	ggtaa	agact	tgga	gtttac	aatct	atgat	gatgat	gatg	120
tgtct	ccatt	cctgga	aggt	cttga	agaaa	gaccac	agag	aaagg	cacag	cctg	ctcaac	180
ctgct	gatga	acctg	cagaa	aagg	ctgatg	aacca	atgga	acatta	agtg	ataag	ccagt	240
ctatat	atgt	attat	caaat	atgta	agaat	acagg	cacca	catact	gatg	acaata	aatct	300
atact	tttgaa	ccaaa	agttg	cagag	tggg	gaatg	ctatg	ttttag	gaat	cagt	ccagat	360
gtgag	ttttt	tccaag	caac	ctcact	gaaa	cctata	tataat	ggaata	catt	tttctt	ttgaa	420
agggt	ctgta	taatca										436

&lt;210&gt; 317

&lt;211&gt; 196

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

<400> 317  
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 gctgctggct tgcagtgcgc gtgcacgtgg agagctgggt cccggagatt ggacggcctg 120  
 atgtccctc cctgcccctg gtccagggaa gctggccgag ggtcctggct cctgaggggc 180  
 atctgcccct ccccca 196

<210> 318  
 <211> 381  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(381)  
 <223> n = A,T,C or G

<400> 318  
 gacgcttngg ccgtaacgat gatcggagac atcctgctgt tccggacggt gctgatgaat 60  
 gccggggcgg tgctgaactt taagctgaaa aagaaggaca cncagggcct tggggaggag 120  
 tncagggagc ccaacacagg tgacaacatc cgggaattct tgctgancct cagatacttt 180  
 cnaatcttca tcnccctgtg gaacatcttc atgatgttct gcatgattgt gctgntcggc 240  
 tcttgaatcc cancgatgaa accannaact cactttcccg ggatgccgan tctccattcc 300  
 tccattcctg atgacttcaa naatgttttt gaccaaaaaa ccgacaacct tcccagaaag 360  
 tccaagctcg tgggtggngg a 381

<210> 319  
 <211> 506  
 <212> DNA  
 <213> Homo sapien

<400> 319  
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 tttgtaaata cctttgttat aattgatagg atacatcttg gacatggaat tgttaagcca 120  
 cctctgagca gtgtatgtca ggacttggtc attaggttgg cagcagaggg gcagaaggaa 180  
 ttatacaggt agagatgtat gcagatgtgt ccataatgtt ccatatttac attttgatag 240  
 ccattgatgt atgcatctct tggctgtact ataagaacac attaatcaa tggaaataca 300  
 ctttgctaat attttaattg tatagatctg ctaatgaatt ctcttaaaaa catactgtat 360  
 tctgttgctg tgtgtttcat tttaaattga gcattaaggg aatgcagcat ttaaatcaga 420  
 actctgccaa tgcttttatc tagaggcgtg ttgccatttt tgtcttatat gaaatttctg 480  
 tccaagaaa ggcaggatta catctt 506

<210> 320  
 <211> 351  
 <212> DNA  
 <213> Homo sapien

<400> 320  
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 cggtagtaac tttgtgttat gaatcacatg aaagcatgga atcttatgaa cttaatccct 120  
 tcattaacag gagaaatgca aataccttca tatcccttca gcagagatgg agagctaaag 180  
 tccaagagag gatccgagaa cgctctaagc ctgtccacga gctcaatagg gaagcctgtg 240  
 atgactacag actttgcgaa cgctacgcca tggtttatgg atacaatgct gcctataatc 300  
 gctacttcag gaagcgccga gggaccaaact gagactgagg gaagaaaaaa a 351

<210> 321

&lt;211&gt; 421

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 321

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ccagaaactc	attgaagtgg	acgatgaacg	caaacttcgt	actttctatg	agaagcgtat	120
ggccacagaa	gttgctgctg	acgctctggg	tgaagaatgg	aagggttatg	tggccgaat	180
cagtgggtggg	aacgacaaac	aaggtttccc	catgaagcag	ggtgtcttga	cccatggccg	240
tgtccgcctg	ctactgagta	aggggcattc	ctgttacaga	ccaaggagaa	ctggagaaaag	300
aaagagaaaa	tcagttcgtg	gttgcatgtg	ggatgcaaat	ctgagcggtc	tcaacttggg	360
tattgtaaaa	aaaggagaga	aggatattcc	tggactgact	gatactacag	tgcctcgccg	420
c						421

&lt;210&gt; 322

&lt;211&gt; 521

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 322

agcagctctc	ctgccacagc	tcctcacccc	ctgaaaatgt	tcgcctgctc	caagtttgctc	60
tcctactccct	ccttggtcaa	gagcacctca	cagctgctga	gccgtccgct	atctgcagtg	120
gtgctgaaac	gaccggagat	actgacagat	gagagcctca	gcagcttggc	agtctcatgt	180
ccccttacct	cacttgctctc	tagccgcagc	ttccaaacca	gcgccatttc	aagggacatc	240
gacacagcag	ccaagttcat	tggagctggg	gctgccacag	ttgggggtggc	tggttctggg	300
gctgggattg	gaactgtgtt	tgggagcctc	atcatttggtt	atgccaggaa	cccttctctg	360
aagcaacagc	tcttctccta	cgccattctg	ggctttgccc	tctcggaggc	catggggctc	420
ttttgtctga	tggtagcctt	tctcatcctc	tttgccatgt	gaaggagccg	tctccacctc	480
ccatagttct	cccgcgtctg	gttgggccccg	tgtgttcctt	t		521

&lt;210&gt; 323

&lt;211&gt; 435

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 323

ccgaggctgc	acgcgtgaga	cttctccgcc	gcagacgccg	ccgcgatgcg	ctacgtcgcc	60
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atcttgagca	gcgtgggtat	cgaggcggac	gacgaccggc	tcaacaaggt	tatcagttag	180
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cctgctgggtg	gggctgtagc	cgtctctgct	gccccaggct	ctgcagcccc	tgctgctggt	300
tctgccccctg	ctgcagcaga	ggagaagaaa	gatgagaaga	aggaggagtc	tgaagagtca	360
gatgatgaca	tgggatttgg	cctttttgat	taaattcctg	ctccccctgca	aataaagcct	420
ttttacacat	ctcaa					435

&lt;210&gt; 324

&lt;211&gt; 521

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 324

aggagatcga	ctttcgggtgc	ccgcaagacc	agggctggaa	cgccgagatc	acgctgcaga	60
tgggtgcagta	caagaatcgt	caggccatcc	tggcgggtcaa	atccacgcgg	cagaagcagc	120
agcacctggg	ccagcagcag	ccccctcgc	agccgcagcc	gcagccgcag	ctccagcccc	180
aaccccagcc	tcagcctcag	ccgcaacccc	agccccaatc	acaaccccag	cctcagcccc	240

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aaccceaagcc tcagccccag cagctccacc cgtatccgca tccacatcca catccacact 300
ctcatcctca ctgcaccca caccctcacc cgcaccgca tccgcaccaa ataccgcacc 360
cacaccaca gccgcactcg cagccgcacg ggcaccggct tctccgcagc acctccaact 420
ctgcctgaaa ggggcagctc ccgggcaaga caagggtttg aggacttgag gaagtgggac 480
gagcacattt ctattgtctt cacttggatc aaaagcaaaa c 521

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&lt;210&gt; 325

&lt;211&gt; 451

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 325

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attttcattt ccattaacct ggaagctttc atgaatatcc tcttctttta aaacatttta 60
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tatttttact tagattactt tgggaatgag agattgttgt cttgaactct ggcactgtac 180
agtgaatgtg tctgtagtgt tgtagtttg cattaagcat gtataacatt caagtatgtc 240
atccaaataa gaggcataata cattgaattg tttttaatcc tctgacaagt tgactcttcg 300
acccccaccc ccaccaaga cattttaata gtaaatagag agagagagaa gagttaatga 360
acatgaggta gtgttccact ggcaggatga cttttcaata gctcaaatca atttcagtgc 420
ctttatcact tgaattatta acttaatttg a 451

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&lt;210&gt; 326

&lt;211&gt; 421

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (421)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 326

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c 421

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&lt;210&gt; 327

&lt;211&gt; 456

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 327

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 <212> DNA  
 <213> Homo sapien

<400> 328  
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 caaggccatc cgagggcacc tggaaaacaa cccagctctg gagaaactgc tgcctcatat 300  
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<210> 329  
 <211> 278  
 <212> DNA  
 <213> Homo sapien

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<400> 329  
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<210> 330  
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 <212> DNA  
 <213> Homo sapien

<400> 330  
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<210> 331  
 <211> 2820  
 <212> DNA  
 <213> Homo sapiens

<400> 331  
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&lt;210&gt; 332

&lt;211&gt; 2270

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 332

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tcgttgatat caaagacagt tgaaggaaat gaattttgaa acttcacggt gtgccaccct 60
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&lt;210&gt; 333

&lt;211&gt; 2816

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 333

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&lt;210&gt; 334

&lt;211&gt; 2082

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 334

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&lt;210&gt; 335

&lt;211&gt; 4849

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 335

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aaacgaagat cccagatga tgaactgtta tacttaccag tgaggggccg tgagacttat 1260
gaaatgctgt tgaagatcaa agagtccctg gaactcatgc agtaccttcc tcagcacaca 1320
attgaaacgt acaggcaaca gcaacagcag cagcaccagc acttacttca gaaacagacc 1380

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ataaacagaa	atggaaaagca	gagttttcat	taaatccttt	tacctttttt	ttttcttggg	4560
aatcccttaa	aataacagta	tgtgggatat	tgaatgttaa	agggatattt	ttttcttatt	4620
atttttataa	ttgtacaaaa	ttaagcaaat	gttaaaagt	ttatatgctt	tattaatgtt	4680

```

ttcaaaagggt attatacatg tgatacattt ttttaagcttc agtttgottgt cttctgggtac 4740
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gacatgcaat aaaattttaa aaataaataa aaactaatta agaaataaa 4849

```

&lt;210&gt; 336

&lt;211&gt; 1386

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 336

```

atgttgatcc tggaaaacaa tgcccagact caatttagtg agccacagta cacgaacctg 60
gggctcctga acagcatgga ccagcagatt cagaacggct cctcgccac cagtccttat 120
aacacagacc acgcgcagaa cagcgtcacg gcgccctcgc cctacgcaca gccagctcc 180
accttcgatg ctctctctcc atcaccgcc atccctcca acaccgacta cccaggcccc 240
cacagtttcg acgtgtcctt ccagcagtcg agcaccgcc agtcggccac ctggacgtat 300
tccactgaac tgaagaaact ctactgccaa attgcaaaga catgccccat ccagatcaag 360
gtgatgaccc cacctcctca gggagctgtt atccgcgcc tgctgtcta caaaaagct 420
gagcacgtca cggagggtgt gaagcgtgtc cccaaccatg agctgagccg tgaattcaac 480
gagggacaga ttgcccctcc tagtcatttg attcgagtag aggggaacag ccatgccag 540
tatgtagaag atcccatcac aggaagacag agtgtgttg taccttatga gccacccag 600
gttggtactg aattcacgac agtcttgtac aatttcattg gtaacagcag ttgtgttgga 660
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tccactgca cacccccacc tccgtatccc acagattgca gcattgtcag gatctggcaa 1380
gtctga 1386

```

&lt;210&gt; 337

&lt;211&gt; 1551

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 337

```

atgtcccaga gcacacagac aaatgaattc ctcagtccag aggttttcca gcatatctgg 60
gattttctgg aacagcctat atgttcagtt cagcccattg acttgaactt tgtggatgaa 120
ccatcagaag atggtgcgac aaacaagatt gagattagca tggactgtat ccgcatgcag 180
gactcggacc tgagtgaccc catgtggcca cagtacacga acctggggct cctgaacagc 240
atggaccagc agattcagaa cggctcctcg tccaccagtc cctataaac agaccacgcg 300
cagaacagcg tcacggcgcc ctgcgccctac gcacagccca gctccacctt cgatgtctc 360
tctccatcac ccgccatccc ctccaacacc gactaccag gcccgcacag tttcgacgtg 420
tccttcagc agtcgagcac cgccaagtcg gccacctgga cgtattccac tgaactgaag 480
aaactctact gccaaattgc aaagacatgc cccatccaga tcaagggtgat gacccacact 540
cctcagggag ctgttatccg cgccatgcct gtctacaaaa aagctgagca cgtcacggag 600
gtggtgaagc ggtgcccaca ccatgagctg agccgtgaat tcaacgaggg acagattgcc 660
cctcctagtc atttgattcg agtagagggg aacagccatg cccagtatgt agaagatccc 720

```

```

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ccaattttta tcattgttac tctggaaacc agagatgggc aagtcctggg ccgacgctgc 900
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ccacctcgt atccacaga ttgcagcatt gtcaggatct ggcaagtctg a 1551

```

&lt;210&gt; 338

&lt;211&gt; 586

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 338

```

Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln
          5                      10                      15

```

```

Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Arg Asn
          20                      25                      30

```

```

Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser
          35                      40                      45

```

```

Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Pro Thr Phe Asp Ala
          50                      55                      60

```

```

Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro
          65                      70                      75                      80

```

```

His Ser Ser Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala
          85                      90                      95

```

```

Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala
          100                      105                      110

```

```

Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly
          115                      120                      125

```

```

Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr
          130                      135                      140

```

```

Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn
          145                      150                      155                      160

```

```

Glu Gly Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn
          165                      170                      175

```

```

Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val

```

180	185	190
Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val		
195	200	205
Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg		
210	215	220
Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val		
225	230	235 240
Leu Gly Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg		
245	250	255
Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp		
260	265	270
Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr		
275	280	285
His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp		
290	295	300
Glu Leu Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu		
305	310	315 320
Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His		
325	330	335
Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln His Gln His Leu		
340	345	350
Leu Gln Lys Gln Thr Ser Ile Gln Ser Pro Ser Ser Tyr Gly Asn Ser		
355	360	365
Ser Pro Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val		
370	375	380
Ser Gln Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr		
385	390	395 400
Ile Pro Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met		
405	410	415
Pro Met Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro		
420	425	430
Pro Pro Leu Ser Met Pro Ser Thr Ser His Cys Thr Pro Pro Pro Pro		
435	440	445
Tyr Pro Thr Asp Cys Ser Ile Val Ser Phe Leu Ala Arg Leu Gly Cys		
450	455	460
Ser Ser Cys Leu Asp Tyr Phe Thr Thr Gln Gly Leu Thr Thr Ile Tyr		
465	470	475 480



Gln Ile Glu His Tyr Ser Met Asp Asp Leu Ala Ser Leu Lys Ile Pro  
485 490 495

Glu Gln Phe Arg His Ala Ile Trp Lys Gly Ile Leu Asp His Arg Gln  
500 505 510

Leu His Glu Phe Ser Ser Pro Ser His Leu Leu Arg Thr Pro Ser Ser  
515 520 525

Ala Ser Thr Val Ser Val Gly Ser Ser Glu Thr Arg Gly Glu Arg Val  
530 535 540

Ile Asp Ala Val Arg Phe Thr Leu Arg Gln Thr Ile Ser Phe Pro Pro  
545 550 555 560

Arg Asp Glu Trp Asn Asp Phe Asn Phe Asp Met Asp Ala Arg Arg Asn  
565 570 575

Lys Gln Gln Arg Ile Lys Glu Glu Gly Glu  
580 585

<210> 339

<211> 641

<212> PRT

<213> Homo sapiens

<400> 339

Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe  
5 10 15

Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro  
20 25 30

Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn  
35 40 45

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu  
50 55 60

Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser  
65 70 75 80

Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn  
85 90 95

Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln  
100 105 110

Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser  
115 120 125

Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln  
130 135 140

Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys  
 145 150 155 160  
 Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val  
 165 170 175  
 Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr  
 180 185 190  
 Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His  
 195 200 205  
 Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His  
 210 215 220  
 Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro  
 225 230 235 240  
 Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val  
 245 250 255  
 Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser  
 260 265 270  
 Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu  
 275 280 285  
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg  
 290 295 300  
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile  
 305 310 315 320  
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys  
 325 330 335  
 Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys  
 340 345 350  
 Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly  
 355 360 365  
 Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu  
 370 375 380  
 Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln  
 385 390 395 400  
 Gln Gln Gln His Gln His Leu Leu Gln Lys Gln Thr Ser Ile Gln Ser  
 405 410 415  
 Pro Ser Ser Tyr Gly Asn Ser Ser Pro Pro Leu Asn Lys Met Asn Ser  
 420 425 430  
 Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg

435	440	445
Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Ile		
450	455	460
Pro Met Met Gly Thr His Met Pro Met Ala Gly Asp Met Asn Gly Leu		
465	470	475 480
Ser Pro Thr Gln Ala Leu Pro Pro Pro Leu Ser Met Pro Ser Thr Ser		
485	490	495
His Cys Thr Pro Pro Pro Pro Tyr Pro Thr Asp Cys Ser Ile Val Gly		
500	505	510
Phe Leu Ala Arg Leu Gly Cys Ser Ser Cys Leu Asp Tyr Phe Thr Thr		
515	520	525
Gln Gly Leu Thr Thr Ile Tyr Gln Ile Glu His Tyr Ser Met Asp Asp		
530	535	540
Leu Ala Ser Leu Lys Ile Pro Glu Gln Phe Arg His Ala Ile Trp Lys		
545	550	555 560
Gly Ile Leu Asp His Arg Gln Leu His Glu Phe Ser Ser Pro Ser His		
565	570	575
Leu Leu Arg Thr Pro Ser Ser Ala Ser Thr Val Ser Val Gly Ser Ser		
580	585	590
Glu Thr Arg Gly Glu Arg Val Ile Asp Ala Val Arg Phe Thr Leu Arg		
595	600	605
Gln Thr Ile Ser Phe Pro Pro Arg Asp Glu Trp Asn Asp Phe Asn Phe		
610	615	620
Asp Met Asp Ala Arg Arg Asn Lys Gln Gln Arg Ile Lys Glu Glu Gly		
625	630	635 640

Glu

&lt;210&gt; 340

&lt;211&gt; 448

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 340

Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe
5 10 15

Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
20 25 30

Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
35 40 45

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu  
 50 55 60  
 Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser  
 65 70 75 80  
 Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn  
 85 90 95  
 Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln  
 100 105 110  
 Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser  
 115 120 125  
 Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln  
 130 135 140  
 Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys  
 145 150 155 160  
 Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val  
 165 170 175  
 Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr  
 180 185 190  
 Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His  
 195 200 205  
 Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His  
 210 215 220  
 Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro  
 225 230 235 240  
 Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val  
 245 250 255  
 Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser  
 260 265 270  
 Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu  
 275 280 285  
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg  
 290 295 300  
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile  
 305 310 315 320  
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys  
 325 330 335

Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys  
                   340                                  345                                  350

Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly  
                   355                                  360                                  365

Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu  
                   370                                  375                                  380

Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln  
                   385                                  390                                  395                                  400

Gln Gln Gln His Gln His Leu Leu Gln Lys His Leu Leu Ser Ala Cys  
                                   405                                  410                                  415

Phe Arg Asn Glu Leu Val Glu Pro Arg Arg Glu Thr Pro Lys Gln Ser  
                   420                                  425                                  430

Asp Val Phe Phe Arg His Ser Lys Pro Pro Asn Arg Ser Val Tyr Pro  
                   435                                  440                                  445

<210> 341

<211> 356

<212> PRT

<213> Homo sapiens

<400> 341

Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln  
                                   5                                  10                                  15

Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn  
                   20                                  25                                  30

Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser  
                   35                                  40                                  45

Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala  
                   50                                  55                                  60

Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro  
                   65                                  70                                  75                                  80

His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala  
                   85                                  90                                  95

Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala  
                   100                                  105                                  110

Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly  
                   115                                  120                                  125

Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr  
                   130                                  135                                  140

Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn

145		150		155		160
Glu Gly Gln Ile	Ala Pro Pro Ser His	Leu Ile Arg Val	Glu Gly Asn			
	165	170	175			
Ser His Ala Gln	Tyr Val Glu Asp Pro	Ile Thr Gly Arg	Gln Ser Val			
	180	185	190			
Leu Val Pro Tyr	Glu Pro Pro Gln	Val Gly Thr Glu	Phe Thr Thr Val			
	195	200	205			
Leu Tyr Asn Phe	Met Cys Asn Ser	Ser Cys Val Gly	Gly Met Asn Arg			
	210	215	220			
Arg Pro Ile Leu	Ile Ile Val Thr	Leu Glu Thr Arg	Asp Gly Gln Val			
	225	230	235	240		
Leu Gly Arg Arg	Cys Phe Glu Ala	Arg Ile Cys Ala	Cys Pro Gly Arg			
	245	250	255			
Asp Arg Lys Ala	Asp Glu Asp Ser	Ile Arg Lys Gln	Gln Val Ser Asp			
	260	265	270			
Ser Thr Lys Asn	Gly Asp Gly Thr	Lys Arg Pro Ser	Arg Gln Asn Thr			
	275	280	285			
His Gly Ile Gln	Met Thr Ser Ile	Lys Lys Arg Arg	Ser Pro Asp Asp			
	290	295	300			
Glu Leu Leu Tyr	Leu Pro Val Arg	Gly Arg Glu Thr	Tyr Glu Met Leu			
	305	310	315	320		
Leu Lys Ile Lys	Glu Ser Leu Glu	Leu Met Gln Tyr	Leu Pro Gln His			
	325	330	335			
Thr Ile Glu Thr	Tyr Arg Gln Gln	Gln Gln Gln Gln	His Gln His Leu			
	340	345	350			
Leu Gln Lys Gln						
	355					

&lt;210&gt; 342

&lt;211&gt; 680

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 342

Met Asn Phe Glu	Thr Ser Arg Cys	Ala Thr Leu Gln	Tyr Cys Pro Asp
	5	10	15
Pro Tyr Ile Gln	Arg Phe Val Glu	Thr Pro Ala His	Phe Ser Trp Lys
	20	25	30
Glu Ser Tyr Tyr	Arg Ser Thr Met	Ser Gln Ser Thr	Gln Thr Asn Glu
	35	40	45

Phe Leu Ser Pro Glu Val Phe Gln His Ile Trp Asp Phe Leu Glu Gln  
 50 55 60  
 Pro Ile Cys Ser Val Gln Pro Ile Asp Leu Asn Phe Val Asp Glu Pro  
 65 70 75 80  
 Ser Glu Asp Gly Ala Thr Asn Lys Ile Glu Ile Ser Met Asp Cys Ile  
 85 90 95  
 Arg Met Gln Asp Ser Asp Leu Ser Asp Pro Met Trp Pro Gln Tyr Thr  
 100 105 110  
 Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn Gly Ser  
 115 120 125  
 Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser Val Thr  
 130 135 140  
 Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala Leu Ser  
 145 150 155 160  
 Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro His Ser  
 165 170 175  
 Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala Thr Trp  
 180 185 190  
 Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala Lys Thr  
 195 200 205  
 Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly Ala Val  
 210 215 220  
 Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr Glu Val  
 225 230 235 240  
 Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn Glu Gly  
 245 250 255  
 Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn Ser His  
 260 265 270  
 Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val Leu Val  
 275 280 285  
 Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val Leu Tyr  
 290 295 300  
 Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg Arg Pro  
 305 310 315 320  
 Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val Leu Gly  
 325 330 335

Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg Asp Arg  
 340 345 350  
 Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp Ser Thr  
 355 360 365  
 Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr His Gly  
 370 375 380  
 Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp Glu Leu  
 385 390 395 400  
 Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu Leu Lys  
 405 410 415  
 Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His Thr Ile  
 420 425 430  
 Glu Thr Tyr Arg Gln Gln Gln Gln Gln Gln His Gln His Leu Leu Gln  
 435 440 445  
 Lys Gln Thr Ser Ile Gln Ser Pro Ser Ser Tyr Gly Asn Ser Ser Pro  
 450 455 460  
 Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val Ser Gln  
 465 470 475 480  
 Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr Ile Pro  
 485 490 495  
 Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met Pro Met  
 500 505 510  
 Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro Pro Pro  
 515 520 525  
 Leu Ser Met Pro Ser Thr Ser Gln Cys Thr Pro Pro Pro Pro Tyr Pro  
 530 535 540  
 Thr Asp Cys Ser Ile Val Ser Phe Leu Ala Arg Leu Gly Cys Ser Ser  
 545 550 555 560  
 Cys Leu Asp Tyr Phe Thr Thr Gln Gly Leu Thr Thr Ile Tyr Gln Ile  
 565 570 575  
 Glu His Tyr Ser Met Asp Asp Leu Ala Ser Leu Lys Ile Pro Glu Gln  
 580 585 590  
 Phe Arg His Ala Ile Trp Lys Gly Ile Leu Asp His Arg Gln Leu His  
 595 600 605  
 Glu Phe Ser Ser Pro Ser His Leu Leu Arg Thr Pro Ser Ser Ala Ser  
 610 615 620  
 Thr Val Ser Val Gly Ser Ser Glu Thr Arg Gly Glu Arg Val Ile Asp



625                      630                      635                      640  
 Ala Val Arg Phe Thr Leu Arg Gln Thr Ile Ser Phe Pro Pro Arg Asp  
                                 645                      650                      655  
 Glu Trp Asn Asp Phe Asn Phe Asp Met Asp Ala Arg Arg Asn Lys Gln  
                                 660                      665                      670  
 Gln Arg Ile Lys Glu Glu Gly Glu  
                                 675                      680  
  
 <210> 343  
 <211> 461  
 <212> PRT  
 <213> Homo sapiens  
  
 <400> 343  
 Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln  
                                 5                      10                      15  
 Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn  
                                 20                      25                      30  
 Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser  
                                 35                      40                      45  
 Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala  
                                 50                      55                      60  
 Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro  
                                 65                      70                      75                      80  
 His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala  
                                 85                      90                      95  
 Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala  
                                 100                      105                      110  
 Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly  
                                 115                      120                      125  
 Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr  
                                 130                      135                      140  
 Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn  
                                 145                      150                      155                      160  
 Glu Gly Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn  
                                 165                      170                      175  
 Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val  
                                 180                      185                      190  
 Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val  
                                 195                      200                      205

Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg  
 210 215 220  
 Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val  
 225 230 235 240  
 Leu Gly Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg  
 245 250 255  
 Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp  
 260 265 270  
 Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr  
 275 280 285  
 His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp  
 290 295 300  
 Glu Leu Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu  
 305 310 315 320  
 Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His  
 325 330 335  
 Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln His Gln His Leu  
 340 345 350  
 Leu Gln Lys Gln Thr Ser Ile Gln Ser Pro Ser Ser Tyr Gly Asn Ser  
 355 360 365  
 Ser Pro Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val  
 370 375 380  
 Ser Gln Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr  
 385 390 395 400  
 Ile Pro Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met  
 405 410 415  
 Pro Met Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro  
 420 425 430  
 Pro Pro Leu Ser Met Pro Ser Thr Ser His Cys Thr Pro Pro Pro Pro  
 435 440 445  
 Tyr Pro Thr Asp Cys Ser Ile Val Arg Ile Trp Gln Val  
 450 455 460

&lt;210&gt; 344

&lt;211&gt; 516

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 344

Met	Ser	Gln	Ser	Thr	Asn	Glu	Phe	Leu	Ser	Pro	Glu	Val	Phe			
				5				10					15			
Gln	His	Ile	Trp	Asp	Phe	Leu	Glu	Gln	Pro	Ile	Cys	Ser	Val	Gln	Pro	
			20					25					30			
Ile	Asp	Leu	Asn	Phe	Val	Asp	Glu	Pro	Ser	Glu	Asp	Gly	Ala	Thr	Asn	
		35					40					45				
Lys	Ile	Glu	Ile	Ser	Met	Asp	Cys	Ile	Arg	Met	Gln	Asp	Ser	Asp	Leu	
	50					55					60					
Ser	Asp	Pro	Met	Trp	Pro	Gln	Tyr	Thr	Asn	Leu	Gly	Leu	Leu	Asn	Ser	
65					70					75					80	
Met	Asp	Gln	Gln	Ile	Gln	Asn	Gly	Ser	Ser	Ser	Thr	Ser	Pro	Tyr	Asn	
				85					90					95		
Thr	Asp	His	Ala	Gln	Asn	Ser	Val	Thr	Ala	Pro	Ser	Pro	Tyr	Ala	Gln	
			100					105					110			
Pro	Ser	Ser	Thr	Phe	Asp	Ala	Leu	Ser	Pro	Ser	Pro	Ala	Ile	Pro	Ser	
			115				120					125				
Asn	Thr	Asp	Tyr	Pro	Gly	Pro	His	Ser	Phe	Asp	Val	Ser	Phe	Gln	Gln	
	130					135					140					
Ser	Ser	Thr	Ala	Lys	Ser	Ala	Thr	Trp	Thr	Tyr	Ser	Thr	Glu	Leu	Lys	
145					150					155					160	
Lys	Leu	Tyr	Cys	Gln	Ile	Ala	Lys	Thr	Cys	Pro	Ile	Gln	Ile	Lys	Val	
				165					170					175		
Met	Thr	Pro	Pro	Pro	Gln	Gly	Ala	Val	Ile	Arg	Ala	Met	Pro	Val	Tyr	
			180					185					190			
Lys	Lys	Ala	Glu	His	Val	Thr	Glu	Val	Val	Lys	Arg	Cys	Pro	Asn	His	
		195					200					205				
Glu	Leu	Ser	Arg	Glu	Phe	Asn	Glu	Gly	Gln	Ile	Ala	Pro	Pro	Ser	His	
	210					215					220					
Leu	Ile	Arg	Val	Glu	Gly	Asn	Ser	His	Ala	Gln	Tyr	Val	Glu	Asp	Pro	
225					230					235					240	
Ile	Thr	Gly	Arg	Gln	Ser	Val	Leu	Val	Pro	Tyr	Glu	Pro	Pro	Gln	Val	
				245					250					255		
Gly	Thr	Glu	Phe	Thr	Thr	Val	Leu	Tyr	Asn	Phe	Met	Cys	Asn	Ser	Ser	
			260					265					270			
Cys	Val	Gly	Gly	Met	Asn	Arg	Arg	Pro	Ile	Leu	Ile	Ile	Val	Thr	Leu	
		275					280					285				
Glu	Thr	Arg	Asp	Gly	Gln	Val	Leu	Gly	Arg	Arg	Cys	Phe	Glu	Ala	Arg	

290	295	300
Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile		
305	310	315 320
Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys		
	325	330 335
Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys		
	340	345 350
Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly		
	355	360 365
Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu		
	370	375 380
Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln		
385	390	395 400
Gln Gln Gln His Gln His Leu Leu Gln Lys Gln Thr Ser Ile Gln Ser		
	405	410 415
Pro Ser Ser Tyr Gly Asn Ser Ser Pro Pro Leu Asn Lys Met Asn Ser		
	420	425 430
Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg		
	435	440 445
Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Ile		
	450	455 460
Pro Met Met Gly Thr His Met Pro Met Ala Gly Asp Met Asn Gly Leu		
465	470	475 480
Ser Pro Thr Gln Ala Leu Pro Pro Pro Leu Ser Met Pro Ser Thr Ser		
	485	490 495
His Cys Thr Pro Pro Pro Pro Tyr Pro Thr Asp Cys Ser Ile Val Arg		
	500	505 510
Ile Trp Gln Val		
	515	

&lt;210&gt; 345

&lt;211&gt; 1800

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 345

ggcgcctcatt gccactgcag tgactaaagc tgggaagacg ctgggtcagtt cacctgcccc 60  
 actgggttggt ttttaaacaa attctgatac aggcgacatc ctactgacc gagcaaagat 120  
 tgacattcgt atcatcactg tgcaccattg gcttctaggc actccagtgg ggtaggagaa 180

```

ggagggtctga aaccctcgca gagggatctt gccctcattc tttgggtctg aaacactggc 240
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tttcatcggg ggtgtcaaca aacactccac cagcatcggg aagggtgtgga tcacagtcac 360
ctttatcttc cgagtcacga tcttagtggt ggctgcccag gaagtgtggg gtgacgagca 420
agaggacttc gtctgcaaca cactgcaacc gggatgcaaa aatgtgtgct atgaccactt 480
tttcccggtg tcccacatcc ggctgtgggc cctccagctg atcttcgtct ccaccccagc 540
gctgctgggt gccatgcatg tggcctacta caggcacgaa accactcgca agttcaggcg 600
aggagagaag aggaatgatt tcaaagacat agaggacatt aaaaagcaca aggttcggat 660
agaggggtcg ctgtggtgga cgtacaccag cagcatcttt ttccgaatca tctttgaagc 720
agcctttatg tatgtgtttt acttccttta caatgggtac cacctgccct gggtgttgaa 780
atgtgggatt gacccctgcc ccaaccttgt tgactgcttt atttctaggc caacagagaa 840
gaccgtgttt accatcttta tgatttctgc gtctgtgatt tgcattgctg ttaacgtggc 900
agagttgtgc tacctgctgc tgaaagtgtg ttttaggaga tcaaagagag cacagacgca 960
aaaaaatcac cccaatcatg ccctaaagga gagtaagcag aatgaaatga atgagctgat 1020
ttcagatagt ggtcaaaatg caatcacagg tttcccaagc taaacatttc aaggtaaaat 1080
gtagctgcgt cataaggaga cttctgtctt ctccagaagg caataccaac ctgaaagtgc 1140
cttctgtagc ctgaagagtt tgtaaataac tttcataata aatagacact tgagttaact 1200
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ggctctatct tgtaaataat gttttgcatt gtctgttggc aaatttgtga actgtcatga 1620
tacgcttaag gtgggaaagt gttcattgca caatatattt ttactgcttt ctgaatgtag 1680
acggaacagt gtggaagcag aaggcttttt taactcatcc gtttgccga tcgttgacga 1740
ccactgggag atgtggatgt ggttgccctc ttttgctcgt ccccggtggc taacccttct 1800

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&lt;210&gt; 346

&lt;211&gt; 261

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 346

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Met Asp Trp Gly Thr Leu His Thr Phe Ile Gly Gly Val Asn Lys His
          5                      10                      15

```

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Ser Thr Ser Ile Gly Lys Val Trp Ile Thr Val Ile Phe Ile Phe Arg
          20                      25                      30

```

```

Val Met Ile Leu Val Val Ala Ala Gln Glu Val Trp Gly Asp Glu Gln
          35                      40                      45

```

```

Glu Asp Phe Val Cys Asn Thr Leu Gln Pro Gly Cys Lys Asn Val Cys
          50                      55                      60

```

```

Tyr Asp His Phe Phe Pro Val Ser His Ile Arg Leu Trp Ala Leu Gln
          65                      70                      75                      80

```

```

Leu Ile Phe Val Ser Thr Pro Ala Leu Leu Val Ala Met His Val Ala
          85                      90                      95

```

```

Tyr Tyr Arg His Glu Thr Thr Arg Lys Phe Arg Arg Gly Glu Lys Arg
          100                     105                     110

```

Asn Asp Phe Lys Asp Ile Glu Asp Ile Lys Lys His Lys Val Arg Ile  
 115 120 125  
 Glu Gly Ser Leu Trp Trp Thr Tyr Thr Ser Ser Ile Phe Phe Arg Ile  
 130 135 140  
 Ile Phe Glu Ala Ala Phe Met Tyr Val Phe Tyr Phe Leu Tyr Asn Gly  
 145 150 155 160  
 Tyr His Leu Pro Trp Val Leu Lys Cys Gly Ile Asp Pro Cys Pro Asn  
 165 170 175  
 Leu Val Asp Cys Phe Ile Ser Arg Pro Thr Glu Lys Thr Val Phe Thr  
 180 185 190  
 Ile Phe Met Ile Ser Ala Ser Val Ile Cys Met Leu Leu Asn Val Ala  
 195 200 205  
 Glu Leu Cys Tyr Leu Leu Leu Lys Val Cys Phe Arg Arg Ser Lys Arg  
 210 215 220  
 Ala Gln Thr Gln Lys Asn His Pro Asn His Ala Leu Lys Glu Ser Lys  
 225 230 235 240  
 Gln Asn Glu Met Asn Glu Leu Ile Ser Asp Ser Gly Gln Asn Ala Ile  
 245 250 255  
 Thr Gly Phe Pro Ser  
 260

&lt;210&gt; 347

&lt;211&gt; 1740

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 347

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 ttcgtggact gcccgacga gagctgggccc ctcaaggcca tcgaggcgct ttcaggtaaa 180  
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 cggaaacttc agatacgaaa tatcccgccct catttacagt gggaggtgct ggatagttta 300  
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 gttgtaaagt taacctattc cagtaaggac caagctagac aagcactaga caaactgaat 420  
 ggatttcagt tagagaattt caccttgaaa gtacccata tccctgatga aacggccgcc 480  
 cagcaaaacc ccttgacga gcccgagggt cgcggggggt ttgggcagag gggctcctca 540  
 aggcaggggt ctccaggatc cgtatccaag cagaaacat gtgatttgcc tctgcgcctg 600  
 ctgggttcca cccaatttgt tggagccatc ataggaaaag aaggtgccac cattcggaac 660  
 atcaccaaac agaccagtc taaaatcgat gtccaccgta aagaaaatgc gggggctgct 720  
 gagaagtcca ttactatcct ctctactcct gaaggcacct ctgcggcttg taagtctatt 780  
 ctggagatta tgcataagga agctcaagat ataaaattca cagaagagat ccccttgaag 840  
 atttttagctc ataataactt tgttggacgt cttattggta aagaaggaag aaatcttaaa 900  
 aaaattgagc aagacacaga cactaaaatc acgatatctc cattgcagga attgacgctg 960

tataatccag aacgcactat tacagttaaa ggcaatgttg agacatgtgc caaagctgag 1020  
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caagcacatt taattcctgg attaaatctg aacgccttgg gtctgttccc acccacttca 1140  
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gagcaatcag aaacgggagac tgttcacatctg tttatcccag ctctatcagt cggtgccatc 1260  
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gaggctcagt tcaaggctca gggaagaatt tatggaaaaa ttaaagaaga aaactttgtt 1440  
agtctaaag aagaggtgaa acttgaagct catatcagag tgccatcctt tgctgctggc 1500  
agagttattg gaaaaggagg caaacgggtg aatgaacttc agaatttgtc aagtgcagaa 1560  
gttgttgtcc ctctgaccca gacacctgat gagaatgacc aagtggttgt caaaataact 1620  
ggtcacttct atgcttgcca gggtgcccag agaaaaattc aggaaattct gactcaggta 1680  
aagcagcacc aacaacagaa ggctctgcaa agtggaccac ctcagtcaag acggaagtaa 1740

<210> 348

<211> 579

<212> PRT

<213> Homo sapiens

<400> 348

Met Asn Lys Leu Tyr Ile Gly Asn Leu Ser Glu Asn Ala Ala Pro Ser  
5 10 15

Asp Leu Glu Ser Ile Phe Lys Asp Ala Lys Ile Pro Val Ser Gly Pro  
20 25 30

Phe Leu Val Lys Thr Gly Tyr Ala Phe Val Asp Cys Pro Asp Glu Ser  
35 40 45

Trp Ala Leu Lys Ala Ile Glu Ala Leu Ser Gly Lys Ile Glu Leu His  
50 55 60

Gly Lys Pro Ile Glu Val Glu His Ser Val Pro Lys Arg Gln Arg Ile  
65 70 75 80

Arg Lys Leu Gln Ile Arg Asn Ile Pro Pro His Leu Gln Trp Glu Val  
85 90 95

Leu Asp Ser Leu Leu Val Gln Tyr Gly Val Val Glu Ser Cys Glu Gln  
100 105 110

Val Asn Thr Asp Ser Glu Thr Ala Val Val Asn Val Thr Tyr Ser Ser  
115 120 125

Lys Asp Gln Ala Arg Gln Ala Leu Asp Lys Leu Asn Gly Phe Gln Leu  
130 135 140

Glu Asn Phe Thr Leu Lys Val Ala Tyr Ile Pro Asp Glu Thr Ala Ala  
145 150 155 160

Gln Gln Asn Pro Leu Gln Gln Pro Arg Gly Arg Arg Gly Leu Gly Gln  
165 170 175

Arg Gly Ser Ser Arg Gln Gly Ser Pro Gly Ser Val Ser Lys Gln Lys





Ser Pro Lys Glu Glu Val Lys Leu Glu Ala His Ile Arg Val Pro Ser  
485 490 495

Phe Ala Ala Gly Arg Val Ile Gly Lys Gly Gly Lys Thr Val Asn Glu  
500 505 510

Leu Gln Asn Leu Ser Ser Ala Glu Val Val Val Pro Arg Asp Gln Thr  
515 520 525

Pro Asp Glu Asn Asp Gln Val Val Val Lys Ile Thr Gly His Phe Tyr  
530 535 540

Ala Cys Gln Val Ala Gln Arg Lys Ile Gln Glu Ile Leu Thr Gln Val  
545 550 555 560

Lys Gln His Gln Gln Gln Lys Ala Leu Gln Ser Gly Pro Pro Gln Ser  
565 570 575

Arg Arg Lys

<210> 349

<211> 207

<212> DNA

<213> Homo sapiens

<400> 349

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gaaaagatga gagaagttac agactctcct gggcgacccc gagagcttac cattcctcag 180  
acttcttcac atggtgctaa cagattt 207

<210> 350

<211> 69

<212> PRT

<213> Homo sapiens

<400> 350

Met Trp Gln Pro Leu Phe Phe Lys Trp Leu Leu Ser Cys Cys Pro Gly  
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Ser Ser Gln Ile Ala Ala Ala Ala Ser Thr Gln Pro Glu Asp Asp Ile  
20 25 30

Asn Thr Gln Arg Lys Lys Ser Gln Glu Lys Met Arg Glu Val Thr Asp  
35 40 45

Ser Pro Gly Arg Pro Arg Glu Leu Thr Ile Pro Gln Thr Ser Ser His  
50 55 60

Gly Ala Asn Arg Phe  
65

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
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- (72) Inventors; and
- (75) Inventors/Applicants (*for US only*): WANG, Tongtong [US/US]; 8049 NE 28th Street, Medina, WA 98039 (US). FAN, Liqun [CN/US]; 14116 SE 46th Street, Bellevue, WA 98006 (US).
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- (88) Date of publication of the international search report:  
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(54) Title: COMPOUNDS AND METHODS FOR THERAPY AND DIAGNOSIS OF LUNG CANCER

(57) Abstract: Compounds and methods for the treatment and diagnosis of lung cancer are provided. The inventive compounds include polypeptides containing at least a portion of a lung tumor protein. Vaccines and pharmaceutical compositions for immunotherapy of lung cancer comprising such polypeptides, or DNA molecules encoding such polypeptides, are also provided, together with DNA molecules for preparing the inventive polypeptides.

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 00/08896

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/47 C12N15/12 C12N15/10 C12N15/62 C07K16/30  
G01N33/53 C12N15/11 C12Q1/68 A61K39/395 A61K38/17  
A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BRASS N ET AL: "Translation initiation factor eIF-4gamma is encoded by an amplified gene and induces an immune response in squamous cell lung carcinoma" HUMAN MOLECULAR GENETICS,GB,OXFORD UNIVERSITY PRESS, SURREY, vol. 6, no. 1, January 1997 (1997-01), pages 33-39, XP002112603 ISSN: 0964-6906 the whole document --- -/--	1,11,17, 18,21, 22,29, 40-53

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

5 October 2000

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# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/08896

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BALDI A ET AL: "DIFFERENTIAL EXPRESSION OF RB2/P130 AND P107 IN NORMAL HUMAN TISSUES AND IN PRIMARY LUNG CANCER" CLINICAL CANCER RESEARCH,US,THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, vol. 3, no. 10, October 1997 (1997-10), pages 1691-1697, XP002910343 ISSN: 1078-0432 the whole document ---	1,11, 40-47, 54,56,57
X	WO 98 35985 A (ELECTROPHORETICS INTERNATIONAL ;HANASH SAMIR M (US)) 20 August 1998 (1998-08-20) the whole document ---	1,11,17, 21,54,57
X	WO 96 30389 A (MILLENNIUM PHARM INC) 3 October 1996 (1996-10-03)  the whole document page 10, line 15 -page 12, line 10 ---	1,9-11, 17,18, 40-60
X	DATABASE EMBL NUCLEOTIDE AND PROTEIN SEQUENCES,17 March 1999 (1999-03-17), XP002149009 HINXTON, GB AC = AI468638. Soares NhHMPu S1 Homo sapiens cDNA clone IMAGE:2125318 3', mRNA sequence. EST. abstract ---	1,2,5-8, 58,59
X	DATABASE EMBL NUCLEOTIDE AND PROTEIN SEQUENCES,18 April 1997 (1997-04-18), XP002149010 HINXTON, GB AC = AA340797. EST46165 Fetal kidney II Homo sapiens cDNA 3' end, mRNA sequence. EST. abstract ---	1,2,5-8, 58,59
X	EP 0 695 760 A (HOFFMANN LA ROCHE) 7 February 1996 (1996-02-07)  the whole document ---	1,9-11, 18, 40-47, 54-57
X	WO 94 06929 A (MERCK PATENT GMBH ;STAHEL ROLF (CH)) 31 March 1994 (1994-03-31) abstract page 2, line 6-32 page 3, line 5-14 ---	1,11,54, 57

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/08896

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96 28473 A (MEDENICA RAJKO D) 19 September 1996 (1996-09-19)  abstract page 2, line 15 -page 3, line 18 page 4, line 1-30  ---	1,11,17, 18,21, 22,35-47
X	WO 98 46788 A (KUFRER PETER ;MICROMET GMBH (DE); ZIPPELIUS ALFRED (DE)) 22 October 1998 (1998-10-22) abstract page 1-10; examples 1-4,6  ---	1,18, 48-53, 58-60
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X	WO 97 07244 A (US GOVERNMENT) 27 February 1997 (1997-02-27) the whole document  ---	1
X	MARSHALL A AND HODGSON J: "DNAchips: an array of possibilities" NATURE BIOTECHNOLOGY, vol. 16, January 1998 (1998-01), pages 27-31, XP002917754 the whole document  ---	1
X	RAMSEY GRAHAM: "DNA chips: state of the art" NATURE BIOTECHNOLOGY, vol. 16, January 1998 (1998-01), pages 40-44, XP002917751 the whole document  ---	1
A	WO 91 18926 A (FORSGREN ARNE) 12 December 1991 (1991-12-12) cited in the application page 5, line 22-35  ---	14,25
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## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 00/08896

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>LELIEVRE D ET AL: "STRUCTURAL PROPERTIES OF CHIMERIC PEPTIDES CONTAINING A T-CELL EPITOPE LINKED TO A FUSION PEPTIDE AND THEIR IMPORTANCE FOR IN VIVO INDUCTION OF CYTOTOXIC T-CELL RESPONSES"</p> <p>EUROPEAN JOURNAL OF BIOCHEMISTRY, BERLIN, DE, vol. 249, no. 3, 1997, pages 895-904, XP000929575</p> <p>ISSN: 0014-2956</p> <p>the whole document</p> <p>---</p>	12,14,25
A	<p>HOGAN KEVIN T ET AL: "The peptide recognized by HLA-A68.2-restricted, squamous cell carcinoma of the lung-specific cytotoxic T lymphocytes is derived from a mutated elongation factor 2 gene."</p> <p>CANCER RESEARCH, vol. 58, no. 22, 15 November 1998 (1998-11-15), pages 5144-5150, XP000946579</p> <p>ISSN: 0008-5472</p> <p>the whole document</p> <p>---</p>	14,25
A	<p>VISSEREN M J W ET AL: "IDENTIFICATION OF HLA-A 0201-RESTRICTED CTL EPITOPES ENCODED BY THE TUMOR-SPECIFIC MAGE-2 GENE PRODUCT"</p> <p>INTERNATIONAL JOURNAL OF CANCER, NEW YORK, NY, US, vol. 73, no. 1, 1997, pages 125-130, XP000914539</p> <p>ISSN: 0020-7136</p> <p>the whole document</p> <p>---</p>	14,25
P,X	<p>WO 99 47674 A (CORIXA CORP)</p> <p>23 September 1999 (1999-09-23)</p> <p>cited in the application</p> <p>SEQ.ID.N.1</p> <p>page 1, last paragraph -page 32, paragraph 1</p> <p>---</p>	1-60
P,X	<p>WO 99 38973 A (CORIXA CORP)</p> <p>5 August 1999 (1999-08-05)</p> <p>page 1, line 28 -page 4, line 15</p> <p>page 16, line 12 -page 17, line 10</p> <p>page 18, line 14 -page 34, line 15</p> <p>---</p> <p>-/--</p>	1-60

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/08896

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WANG TONGTONG ET AL: "Identification of genes differentially over-expressed in lung squamous cell carcinoma using combination of cDNA subtraction and microarray analysis." ONCOGENE, vol. 19, no. 12, 16 March 2000 (2000-03-16), pages 1519-1528, XP000951444 ISSN: 0950-9232 the whole document	1-60
T	----- HENDERSON R A ET AL: "Identification of lung tumor antigens for cancer immunotherapy: Immunological and molecular approaches." IMMUNOLOGICAL INVESTIGATIONS, vol. 29, no. 2, May 2000 (2000-05), pages 87-91, XP000951456 Fourteenth International Convocation on Immunology; Buffalo, New York, USA; October 08-11, 1999 ISSN: 0882-0139 the whole document -----	1-60

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 00/08896

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
**see FURTHER INFORMATION sheet PCT/ISA/210**
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**1-60 all partially**

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.



## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## 1. Claims: Invention 1 : Claims 1-60 all partially.

An isolated polypeptide, comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence as recited in SEQ.ID.N.1 (a) or sequences that hybridize to SEQ.ID.N.1 (b) and the complements of sequences of (a) or (b); as well as an expression vector, a host cell, an antibody, a fusion protein, a pharmaceutical composition, a vaccine, oligonucleotides and diagnostic kits thereof.

## 2. Claims: Inventions 2 to 130 : Claims 1-60, all partially.

Same as invention 1, but according to each single sequence as recited in claim 1  
(SEQ.ID.N.1-3,6-8,10-13,15-27,29,30,32,34-49,51,52,54,55,57-59,61-69,71,73,74,77,78,80-82,84,86-96,107-109,111,113,125,127-129,131-133,142,144,148-151,153,154,157,158,160,167,168,171,173,175,179,182,184-186,188-191,193,194,198-207,209,210,213,214,217,220-224,253,254-258,260,262-264,270,272,275,276,279-281,286,287,291,293,295,296,300,302,308-310,313,315-317,323,345,347 and 349)

and as recited in claim 3  
(SEQ.ID.N.110,112,114,152,155,156,159,161,165,166,169,170,172,174,176,226-252,346,348 and 350)

starting from the second in the list: SEQ.ID.N.2 and following with SEQ.ID.N.3, SEQ.ID.N.6, etc... and ending with SEQ.ID.N.350.

and with the provision that sequences tht belong to the same antigen has been counted as one invention (see below)

## 3. Claims: Inventions 131-258 : Claims 25-61 all partially

A vaccine comprising an antigen-presenting cell that expresses a polypeptide comprising at least an immunogenic portion of a lung tumor protein wherein the protein comprises an amino acid sequence encoded by a polynucleotide sequence as recited in claim 25  
(SEQ.ID.N.4,5,9,14,28,31,33,50,53,56,60,70,72,75,76,79,83,85,97-106,115-124,126,130,134-141,143,145-147,162-164,177,178,180,181,183,187,192,195-197,208,211,212,215,216,218,219,255-259,261,265-269,271,273,274,277,278,282-285,288-290,292,294,297-299,301,303-307,311,312,314,319-322 and 324-337) and kits for diagnostic thereof.

Same as invention 130, but according to each single sequence as recited in claim 25 and not included in claim 1, starting from the SEQ.ID.N.4 and following with SEQ.ID.N.5, SEQ.ID.N.9, etc... and ending with SEQ.ID.N.337.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

and with the provision that sequences tht belong to the same antigen has been counted as one invention (see below)

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

Continuation of Box I.1

Although claims 21, 22, 29-31, 34, and 37-39 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Although claim(s) 40-53 are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No  
PCT/US 00/08896

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Information on patent family members

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